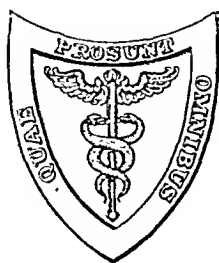


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ORIGINAL ARTICLES.

PAROXYSMAL PULMONARY ŒDEMA AND ITS TREATMENT.

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THE condition designated paroxysmal pulmonary œdema cannot well be mistaken for any other. It comes on very suddenly with little or no premonitory indication and rapidly assumes such alarming characters that the patient and those about him feel that a fatal termination can be a matter of but few minutes. The patient at the very beginning experiences a sense of suffocation or oppression of breathing which speedily becomes extreme. He struggles for breath, and soon becomes additionally oppressed by paroxysms of suppressed cough in which a little frothy and often blood-tinged serous fluid is brought up. Later, larger quantities of the same sort of frothy serum may be expectorated or may literally well up from the lungs. The breathing is merely moist on auscultation or noisy, according to the degree of œdema; in severe attacks it becomes suppressed. When the frothy expectoration has stood for a time in a vessel the bubbles of air disappear, leaving a clear and usually blood-tinged serous fluid.

At the moment of the attack the patient grows suddenly deathly pale and wears the anxious expression of terror of one who fears instant death. The hands, feet, and whole body grow cold and become bathed in a dripping sweat. Later, as the respirations grow more and more difficult, cyanosis becomes associated with the pallor. Extreme cyanosis, however, is uncommon. The pulse, usually extremely weak and rapid in the beginning, may continue so until some relief is afforded. In some of the seizures in cases reported in this series the pulse during the early part

of the paroxysm was almost imperceptible, and improved very gradually as the attack subsided. Occasionally, however, the pulse may be rapid and excited during an attack and may give no evidence of reduced cardiac power. It will be shown later that even in such cases the actual working power of the left ventricle may be diminished, and that the mechanical conditions capable of developing pulmonary œdema may be present despite the seeming strength of the pulse.

At the beginning of the attack the patient is usually nervous and frightened, and this condition may increase with the oppressed breathing and suffocating cough. Later, a certain amount of stupor or partial unconsciousness may develop, but this is unusual. After a time the patient grows easier; warmth returns to the hands, which have been cold and cyanosed; the breathing improves; the moist rales in the chest grow less abundant; color returns to the face; and the pulse grows stronger and less frequent. The majority of paroxysms terminate in this way; in but a small proportion of cases does a fatal termination occur, notwithstanding the extreme violence of the symptoms usually observed. Some patients have, however, died in the first attack; others have survived for a period of months or years, despite repeated seizures. In Lissaman's¹ case there were seventy-two attacks during a period of over two years; and the patient was living at the time of the report. In one of my cases paroxysms have occurred at intervals of weeks or months during the last ten years; and the patient is now in rather better physical condition than after the first attack in 1900.

The distinguishing features, clinically speaking, of the condition that has been referred to are its sudden onset, usually with slight provocation; the evidence of intense pulmonary œdema; the expectoration of quantities of frothy and blood-stained serum; and the repetition of such attacks without intercurrent complicating conditions. These features distinguish this condition from certain other forms of acute pulmonary œdema, which, during their height, may not be especially different in clinical manifestations.

The seizures, as a rule, come on in the evening or after the patient has gone to bed. He may awake from a profound sleep with an oppressed cough, followed by the symptoms described. In some cases, vague apprehensions or unaccountable nervous feelings may precede the attack; but these usually occur only after a repetition of the seizures has made the patient familiar with their character and fearful of their recurrence. Various kinds of excitement, physical or mental, may provoke the attacks; but in a large proportion of cases there is no such cause.

Repeated attacks of the same character may occur at intervals of days or weeks during a long period of time. In one of my cases

¹ *Lancet*, February 8, 1902.

the seizures began over ten years ago and have continued up to the present time at varying intervals. Between attacks the patient may be perfectly well, or more frequently give evidence of some inadequacy of cardiac compensation. In the cases which have terminated fatally the final result has usually been due to increasing cardiac decompensation rather than to the sudden effect of an attack of pulmonary œdema.

It is necessary to point out here some of the other varieties of acute pulmonary œdema met with clinically, so that the limitations of what is intended to be included under the title paroxysmal pulmonary œdema may be more evident.

1. ACUTE ŒDEMA ASSOCIATED WITH OTHER LESIONS OF THE LUNGS. It is a well-known fact that cases of pneumonia or pulmonary tuberculosis may terminate suddenly by the development of an acute œdema affecting a part or all of the lung not involved in the original trouble. The explanation offered for such cases by older writers, and to a large extent still accepted, is that there is a collateral hyperemia or fluxion, resulting from the extent of the original trouble. Another explanation is, however, possible, particularly in cases of acute pneumonia. This is that, as a result of dissemination of the infective cause, an acute inflammatory œdema of the entire lung or of both lungs follows after the original infection. In this condition, there may be a close resemblance in the symptoms to what has been described before; but the history of the case and the circumstances under which the acute œdema arises distinguish this from paroxysmal œdema.

2. ACUTE INFECTIOUS ŒDEMA; ACUTE INFLAMMATORY ŒDEMA; OR ACUTE ŒDEMATOUS INFLAMMATION. This condition, which was originally described by Traube as serous pneumonia, or diffuse congestive pneumonia, may occur in association with certain infectious diseases, such as scarlet fever, smallpox, typhus fever, rheumatism, or influenza, or as a primary infection of the lungs. Its resemblance to vagus pneumonia is too close to be overlooked; and its occurrence in cases of acute cerebral disease, head injuries, or sunstroke is likewise suggestive. Strümpell² alludes to such cases, and mentions the absence of other lesions than the œdematous lung. Hilton Fagge³ and Fowler⁴ describe the same condition. Sahli⁵ insists that this is purely an infectious condition; and Kockel,⁶ in his pathological and bacteriological study of 6 cases following head injury, found a constant association of bacterial invasion and the acute inflammatory lesions. He further states that Thoma believes that most diffuse or extensive œdemas are inflammatory and infectious, and mentions that Ziegler describes

² Text-book on Medicine, second American edition, p. 183.

³ Text-book on Medicine, third edition, i, 1002.

⁵ Archiv f. exper. Pharm. u. Path., 1885, 19.

⁶ Deut. Naturf. und Aerzte, 1896, lxxviii, 30.

⁴ Diseases of the Lungs, p. 281.

such cases as "septic-toxic" œdema. Welch⁷ states that he agrees with Sahli regarding the frequency of infectious inflammatory pulmonary œdemas, basing his opinion upon the systematic bacterial examinations made at all autopsies at the Johns Hopkins Hospital. Not only in irregular and localized œdemas, but also in not a few extensive and even general ones, plate cultures from the lungs showed numerous colonies of bacteria, most frequently streptococci and lanceolate micrococci, so numerous that they must have been in active growth in the lungs. Sudden œdema associated with Bright's disease, described by Dieulefoy⁸ and by other French writers, may, in some cases, belong in this same group, but is possibly susceptible of another explanation, similar to that which will be suggested in the case of paroxysmal œdema.

The clinical manifestations of acute infectious œdema, as I have seen them in some cases of influenza and other infections, do not differ greatly from those of paroxysmal pulmonary œdema, except that there is much less suddenness and vehemence of the symptoms. Certain authors (as Romberg) have mentioned as distinguishing features the fact that there is fever in these cases, and usually a pulse suggestive of increased rather than lessened cardiac action; and undoubtedly these are important points, and may lead to a proper diagnosis. It must, however, be recalled that fever is not invariably present, and that in some instances of paroxysmal pulmonary œdema the pulse-rate does not give evidence of decided cardiac weakness. A more important criterion for distinguishing the two conditions is the tendency to recurrence in the one and the absence of such a tendency in the other. Furthermore, paroxysmal pulmonary œdema, as will be pointed out later, occurs in association with certain other conditions, cardiovascular or renal, and rarely independently of such causes; while infectious œdema may appear in persons previously in perfect health. Later, in the discussion of the pathogenesis of the pulmonary condition in paroxysmal cases, I shall have occasion to point out that infection has been thought of as the important etiological factor. A series of paroxysms would, therefore, necessarily imply a series of successive infections. Such an occurrence is manifestly most unlikely, and all the facts connected with the recurrent paroxysms in cases such as those observed by myself over long periods of time speak strongly against this possibility.

3. ACUTE ŒDEMA ACCOMPANYING RAPID DILATATION OF THE HEART. In cases of acute dilatation of the heart caused by acute myocarditis or degeneration of the heart, considerable œdema of the lungs may develop quite rapidly; and the clinical features at the height of such an attack may be indistinguishable from those

⁷ Quoted by Meltzer, "Œdema," *American Medicine*, viii, Nos. 1 to 5.

⁸ *Path. Int.*, thirteenth edition, T. I., i, 282.

which occur in seizures of paroxysmal œdema such as have been described. The manner of onset and the coincident conditions, however, distinguish such cases from the paroxysmal type; for there is usually a clear history of preceding acute cardiac weakness, and, perhaps, even prior to that, of some infection which has occasioned it. Then, too, physical signs of increasing cardiac weakness and of increasing dilatation of the heart precede the onset of the pulmonary œdema. Thus, it is usually possible to distinguish the two conditions, notwithstanding the fact that at the height of the symptoms they are practically indistinguishable, as cardiac dilatation quite commonly occurs as an incident of the attack in the paroxysmal variety.

While we may thus recognize four types of sudden, or acute, œdema of the lungs, it must be apparent that the first is clearly distinguished from the others mainly by its recurrent character; and for this reason, I have ventured to use the term *paroxysmal pulmonary œdema*. Among other names that have been suggested is acute suffocative pulmonary œdema, but this is less descriptive, because practically all forms of acute œdema are almost equally suffocative in character.

A report of some typical cases will serve to indicate the clinical features.

CASE I.—Mr. E. B., aged seventy years, at the time of his death, in May, 1909, had been under my observation for six or eight years. He had formerly been addicted to the overuse of alcohol, and was an inveterate smoker. He came of a distinctly gouty family, and he himself suffered from a moderate obesity and later from a mild glycosuria which came and went. During the time he was under my observation I recognized the development of increasing arteriosclerosis, and examinations of the urine showed traces or small quantities of albumin and tube casts significant of an increasing interstitial nephritis. The blood pressure was constantly high, and increased with succeeding years. During the last four years of his life the sugar had disappeared from the urine. None was present from January, 1905, up to the time of his death.

The first attack of pulmonary œdema occurred during the winter of 1908, after a somewhat heavy dinner. The patient had gone to the theatre, and while there complained of the heat of the room and of oppression of breathing. He was quickly hurried out before the attack developed, but he could not get to his home, and when I reached him, fifteen minutes later, in an adjoining house, where he had been taken, I found him in the midst of an attack of the most intense severity. The pulse was scarcely palpable, the face was livid, and the skin everywhere icy cold and bedewed with dripping perspiration. The breathing was noisy and the lungs were evidently œdematous throughout. A physician who had

seen him before my arrival had given him a pearl of nitrite of amyl, which was inhaled from a handkerchief with apparently some slight relief. I gave him a hypodermic injection of morphine with atropine, and in a short time he was sufficiently restored to be taken home; but subsequent hypodermic injections of strychnine, nitroglycerin, and atropine were given, as the patient was greatly exhausted. After an hour he fell asleep, and the next day was practically well though much exhausted. After this attack the patient had a succession of similar seizures, probably fifteen in all, none, however, of the intensity of the first, and in each of these the prompt administration of hypodermic injections of morphine, sometimes with and sometimes without atropine, relieved him speedily. The general course of his case, however, was a downhill one, and finally increasing œdema and other evidences of cardiac failure terminated the condition. Toward the end it seemed to me as if he might perish in one of the attacks on account of his generally weakened condition and the progressive deterioration of cardiac strength, but there never was any difficulty in controlling the seizures themselves. The final outcome of the case and the progress was practically the same as that of a case of general arteriosclerosis with cardiac disease unattended with such paroxysms of pulmonary œdema.

CASE II.—Mrs. H. E. R., now aged fifty years, first came under my observation in December, 1900. She had had a severe attack of cardiac disturbance of some sort a short time before that date, and when I first saw her she was still suffering from some of the consequences of a disturbance or a loss of compensation. The principal symptoms were dyspnoea, cough, and other indications of pulmonary congestion. On physical examination I found slight enlargement of the heart and the evidences of mitral stenosis. After the administration of moderate doses of cardiac tonics, compensation became restored and the patient was quite well until February, 1902, when a sudden attack of intense congestion and œdema of the lungs with cardiac weakness occurred in the middle of the night. Another attack occurred in March, 1902, after which she remained free of seizures, although at times not entirely well, until the spring of 1906, when she was greatly reduced by hemorrhoidal bleeding, and in May she had another severe attack of acute œdema. The fifth attack occurred during the summer of 1906, the seventh about six weeks later, the eighth and ninth in October and December of 1908, the tenth in October, 1909, and the eleventh on January 28, 1910. All of these attacks have been of similar character and all occurred during the night. In several the direct cause was sexual excitement. In others the patient has been wakened from sleep with a frightened feeling, which was quickly followed by intense oppression of breathing, a rattling sound in the chest, great weakness and rapidity

of the pulse, and the expectoration of more or less copious amounts of frothy and usually blood-tinged serum. Since the first attack, and up to the latest one, she has had the prompt attendance of a physician, who administered hypodermic injections of morphine with small amounts of atropine, and the result has invariably been a speedy recovery after a single hypodermic dose. In the last attack strychnine and nitroglycerin were used, and though the patient recovered from the attack, the duration was somewhat longer than on previous occasions, and the attack was one of no great severity, having been attended with but little œdema and no frothy expectoration. The first attack of all was described as the most severe of the series, but I cannot give any details regarding it. After the attacks the patient quickly regains her normal condition, but during the ten years she has been under my care there has been the constant evidence of a cardiac defect with slight dyspnoea on exertion and a lowered general vitality. There has been no evidence of progressive loss of power in the heart, and the patient's general condition now is apparently quite as satisfactory as it was in the beginning. The physical signs of mitral stenosis, as is so common in cases of that lesion, are more distinct in the intervals between than during or immediately following attacks. Urinary examinations have shown a slight trace of albumin on a few occasions, but not more than might be attributed to the leukocytes present as a result of some vesical trouble. The latest examination made on the day following her attack of January 28 showed: specific gravity 1018, reaction acid, no albumin, no sugar, no cylindroids or casts, a number of leukocytes, and some uric acid crystals. There has never been any indication in the urinary examinations or symptoms of nephritis.

CASE III.—I. K., aged fifty years, first came under my care in 1901. He had used alcohol periodically to great excess, but not at all during the last year and never subsequently up to the time of his death in 1909. He had, however, continued smoking immoderately, and never limited this at all reasonably until near the end of his life. In 1902 he suffered from an attack of abdominal pain which Dr. J. Chalmers Da Costa and I regarded as due to appendicitis, but we decided it safer to avoid operation on account of certain cardiac symptoms. For some time previous to this date the patient had complained of substernal and precordial oppression, especially on slight exertion, as in walking up moderate hills on his golf course. The pulse was constantly rapid, and more so when he was specially oppressed. The heart sounds were weak but sharp, and the aortic second sound slightly accentuated. There was no cardiac enlargement and no murmur. In 1904 he had considerable anginoid pain, and in the summer another attack of what was regarded as appendicitis. Early in 1905 he had another abdominal attack, with pain most marked in the epigastrium.

Soon after this he complained of a severe headache or neuralgia, which was followed by right homonymous hemianopia affecting the right upper quadrant. Dr. de Schweinitz saw him and reported the condition "right lateral homonymous tetranopia." The vision improved after some time and possibly as a consequence of the use of potassium iodide. Another abdominal attack occurred later in 1905. In the meantime, his precordial distress never was wholly relieved, though it was less severe or he had grown accustomed to it. During the summer of 1907 he had one or two attacks of severe cardiac distress while at some altitude in the Adirondack mountains; and in the spring of 1908 he had the first attack of threatening character. The description of the seizure, given by a friend who was with him, corresponded in every detail with that which would apply to subsequent attacks which I observed. A pellet of morphine and one of nitroglycerin were given, and after some hours relief occurred. I saw the patient the next day and found him in his usual condition, though somewhat used up by his experience of the night before. The cardiac signs were the same as those described. On the following night another attack occurred, and in this he developed a complete right hemiplegia with aphasia. Up to this time I had not seen the patient in an attack, but during the following eighteen months I saw him in several, and in others Dr. Klaer was called.

There was usually little premonition of the attack, but a certain amount of nervousness and mild oppression preceded the paroxysm for a short time. The attack itself set in very suddenly with extreme oppression of breathing, violent palpitation with great weakness of the heart beat and pulse, ashy pallor combined with some cyanosis, and cold sweat. Very soon he would begin to cough in short interrupted paroxysms, bringing up frothy serous fluid of pink color, and in bad seizures the same kind of frothy fluid flowed from his mouth between the coughing attacks. At the height of the attack the lungs were filled throughout with moist rales and the entrance of air was reduced to a minimum. Scarcely any inspiration or expiration could be distinguished.

During the eighteen months following the hemiplegia there were twelve such attacks or distinct beginnings of attacks and a number of milder suggestions. He was under the constant care of a nurse, who had been instructed to give a hypodermic injection of morphine, $\frac{1}{4}$ grain, and atropine, $\frac{1}{250}$ grain, at the first sign of a seizure, to be followed by one of strychnine sulphate, $\frac{1}{20}$ grain, and nitroglycerin, $\frac{1}{100}$ grain, within ten or fifteen minutes, and a repetition of morphine, $\frac{1}{8}$ grain, with atropine, $\frac{1}{250}$ grain, after a half hour if necessary. This plan never failed to abort the attacks within a few minutes and without any actual need for the second or third injection. In two or three of the attacks, when the nurse or members of the family thought the first symptoms merely

nervousness, the attacks got greater headway and relief did not occur as speedily, but even then the patient was relieved in a half hour. The effect of the injections was to cause a rapid improvement in the oppression of breathing, followed by a fuller pulse, returning warmth of the extremities, and diminution in the frothy expectoration. The last four attacks occurred during the summer in Atlantic City, and Dr. Porteous reports that these were of the same character as previous ones, and up to the last one were controlled by a moderately large hypodermic dose of morphine and atropine, which on one or two occasions had to be repeated. The last and fatal attack differed only in being more severe than any previous ones Dr. Porteous had seen. It began while the patient was in a theatre, and possibly the delay in applying treatment may have been responsible for the fatal result. There was no autopsy.

CASE IV.—W. H. S. was admitted to my service at the University Hospital in February, 1905, on account of cough, expectoration, and occasional hemoptysis. The patient was a shipper, aged twenty-two years, who had suffered from articular rheumatism four years ago, had been a moderate user of alcohol and tobacco, but without any other significant history. At this time signs of aortic regurgitation and mitral stenosis were discovered and a suspicious lesion was found at the apex of the left lung. We were never certain that this was a tuberculous lesion, as examination for bacilli was always negative and the cardiac condition could have easily occasioned a localized area of congestion. The patient left the hospital in April and was treated at a sanatorium for tuberculosis, where he remained until September, 1905, having gained considerably in weight, and being then discharged as cured. He attempted to resume his work, but soon noticed a return of blood-tinged sputum, and reentered the hospital in the fall of 1907, with practically the same conditions we had previously found. The patient, however, had increased greatly in weight from the forced feeding, and we were under the impression that this increased weight had exaggerated rather than helped his cardiac difficulties. After a month's stay in the hospital he felt quite well, and was about to go home, when some little excitement incident to his departure from the hospital caused a sudden attack of acute oedema. He had walked from the ward to the elevator, and there was seized with intense dyspnoea and weakness, and was carried back to his bed. A severe attack of acute oedema followed, the respirations increasing to 50, the pulse to 160 per minute. Considerable frothy material welled out of his mouth and he was extremely cyanosed. Repeated injections of camphorated oil, digitalin, and atropine were given. Of the last, doses of $\frac{1}{8}$ grain were given every thirty minutes during four hours, but the attack did not subside for eight hours, after which there was a slight improvement. During this attack it was noted that the cardiac dulness increased to the left

as well as to the right, and as the patient improved the following day this increased dulness seemed to diminish. A second attack occurred two weeks later, and was described as a very severe one. The symptoms were the same as those in the previous seizure. A hypodermic injection of morphine and atropine followed by digitalin and camphorated oil quickly terminated this attack, and the patient's condition was practically normal within a few hours. Five days later a third attack occurred, and promptly yielded to a single injection of morphine and atropine. Three more seizures followed at intervals of a few weeks, after which the patient had no further attacks of this sort. He subsequently developed a fresh cardiac infection with pericarditis, and eventually succumbed to this. Repeated examinations of the urine showed either an absence of albumin or mere traces, and sometimes a few hyaline casts, but more often none at all.

CASE V.—J. G., aged sixty-one years, had first come under my observation early in 1908, after an attack of cardiac palpitation and dyspnoea which had come on during the night. He was sent to the University Hospital, where he has been a patient off and on up to the present time. Examination showed evidences of general arteriosclerosis and chronic interstitial nephritis. The peripheral vessels are sclerosed and tortuous. The blood pressure has varied from 200 to 240 mm. systolic, and 130 to 145 mm. diastolic. There is more or less constant polyuria, and the examinations have shown traces of albumin with hyaline and granular casts. Since his first admission to the hospital there have been a number of attacks similar to the one he described as having occurred before admission. The first of these which occurred in the hospital is described as follows: "The patient was suddenly seized with an attack starting with eructations, followed in a short time by coughing and expectoration of frothy material. Dyspnoea became very marked, making it impossible for him to breathe unless sitting up in bed. A hypodermic injection of morphine caused a relief, but a return of the attack required a second injection." All the subsequent attacks have been similar to this. Their onset has been sudden and without marked premonition. The lungs quickly become moist and breathing seriously oppressed. A hypodermic injection of morphine with atropine quickly terminates the seizures.

On account of the renal condition, the patient has had constant hot packs at intervals of two or three days, and his general condition has remained practically stationary. Lately, however, a slight increase in the frequency of the attacks has been noted, and their sharp demarcation from his average condition has been less distinct, as the breathing remains somewhat oppressed and the lungs slightly congested between the seizures. Some tests as to the relative value of injections of morphine and of morphine and atropine in the recent paroxysm seem to show a moderate advantage in the latter over the former.

The progress of this case has been from a condition of practical comfort for long stretches punctuated by sudden intense seizures, from which the patient quickly returned to his usual condition, to one of more frequent but less severe attacks with a more lasting state of pulmonary congestion and œdema between the paroxysms.

ETIOLOGY. The explanation of paroxysms of sudden pulmonary œdema may be sought (1) in a study of the conditions in which such paroxysms have been encountered, and (2) in the experimental and physiological data bearing upon the question.

1. *Associated Pathological Conditions.* Several authors have summarized the literature of acute pulmonary œdema, and have made tables of the various conditions with which it was associated. Samuel West⁹ mentions as a rough classification of the causes of acute œdema: (1) Acute inflammation; (2) acute collateral fluxion; (3) sudden mechanical obstruction to the vessels; (4) acute fevers; (5) certain poisons; (6) hyperpyrexia; (7) acute nephritis; and (8) paracentesis thoracis; and in the detailed discussion of these groups speaks of various diseases which fall under one or the other of the headings. Riesman¹⁰ mentions, among the associated conditions in reported cases, arteriosclerosis, Bright's disease, heart disease, asthma, acute infectious diseases, pregnancy, paracentesis of the thorax and of the abdomen, angioneurotic œdema, obscure conditions of questionable relationship (hysteria, etc.).

It is evident that the acute œdema which occurs in some of these conditions is not strictly comparable to the paroxysmal type which is under discussion. Thus, the sudden œdema occurring after paracentesis or in some violent infection, such as scarlet fever, very probably results from different causes than those which are operative in the cases in which one paroxysm after another has occurred more or less spontaneously. To say the least, there must be an added factor of etiology that determines such recurrences of œdema, and more probably the etiology is entirely different. In the case of infectious acute œdema, for example, it is very probable that the direct action of the microorganisms upon the pulmonary vessels and the adjacent tissues is the immediate cause, and it is inconceivable that repeated attacks of paroxysmal œdema are due to repeated acute infections. The same thought applies to the probable mechanical disturbances operative in the œdema following paracentesis. It is necessary, therefore, to distinguish the conditions with which acute œdema has been associated as a recurring paroxysmal event from those in which there have been only single attacks. Little help in the direction of solving the question of the etiology of the œdema in the paroxysmal type of cases can

⁹ Diseases of the Organs of Respiration, 1902, i, 242.

¹⁰ AMER. JOUR. MED. SCI., 1907, cxxxiii, 88; Trans. Assoc. Amer. Phys., xxi, 155.

be expected from mere tabulations of all the pathological conditions in which any sort of sudden pulmonary œdema occurred; but in studying the detailed descriptions of the cases which have been reported and upon which the tables are based, the paroxysmal type stands out very prominently. Taking this group alone, it is found that practically all of the cases were instances of cardiac or renal disease, or arteriosclerosis. Young persons without any of these conditions may suffer infectious pulmonary œdema, collateral œdema, or œdema following paracentesis; but the paroxysmal and recurring type has been found almost if not quite exclusively in association with the three conditions named.

So far as my own experience has been concerned, the cases have, with but one exception, been instances of cardiac, renal, or arterial disease attended with high blood pressure, and in the one exceptional case there was a cardiac lesion (mitral stenosis), and each attack of œdema was preceded by a nervous disturbance which doubtless temporarily elevated the systemic blood pressure. In some of the reported cases of recurring pulmonary œdema, unassociated with any of the three pathological conditions referred to, there have been other conditions—pregnancy (Riesman), nervous conditions (Levallée, Levy)—in which temporary or more continuous high pressure may have occurred.

The conditions which stand out most prominently in the cases that I have encountered have been increasing myocardial weakness and high arterial pressure. The occurrence of pulmonary œdema has, therefore, been more common in cases of myocardial than of valvular disease, and in cardiac disease associated with nephritis and arteriosclerosis than in the absence of such an association. The possible significance of these facts may be left for further discussion until the data of experimental investigation have been detailed.

2. *Experimental and Physiological Data.* Professor Wm. H. Welch,¹¹ in 1878, published the results of some experimental studies which have thrown a great deal of light on the pathogenesis of sudden pulmonary œdema. After reviewing various earlier theories he reports his experiments, which were directed to the determination of the possibility of producing pulmonary œdema by obstructions to the outflow of blood from the pulmonary circulation. Some preliminary experiments showed that the adaptability of the heart and circulation is so great that ligation of several of the large branches of the aorta failed to interfere with the work of the left ventricle sufficiently to lower the systemic circulation notably or to occasion pulmonary congestion and œdema. Ligation of the root of the aorta itself or clamping the pulmonary veins did occasion such results, but these procedures cause violent obstructions

¹¹ Archiv f. path. Anat. und Phys., 1878, lxxii, 375.

of the circulation such as have no analogies in ordinary disease. The crucial experiment, to which various less convincing ones led up, was one in which he was able to cause acute œdema of the lungs in rabbits by squeezing the left ventricle between his finger and thumb, thus partially paralyzing it. He concluded that acute pulmonary œdema is due to "a disproportion between the working power of the left ventricle and of the right ventricle of such a character that, the resistance remaining the same, the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." He did not then deny the possibility of another explanation for collateral fluxion with œdema or for infectious œdemas, and in a recent statement (quoted by Meltzer, 1904) specifically admits that a larger proportion of the cases of pulmonary œdema than is generally supposed is due to inflammatory changes in the vascular walls. His earlier experiments, however, conclusively demonstrated the fact that a lessened output of blood from the left ventricle as compared with the right could occasion acute pulmonary œdema. It is of interest to note that in cases of marked interference with the systemic circulation, even involving the distribution of several of the large branches of the aorta, he did not obtain the same result, nor even a notable falling off in arterial pressure, a fact which can be explained only by the reserve power of the heart and the extraordinary capacity for adjustment of the vasomotor apparatus of the systemic circulation. This fact, I believe, has important clinical bearings in connection with the cases of paroxysmal œdema. It cannot be referred to any vasomotor adjustment in the pulmonary circulation, for the reason that the ligatures established mechanical obstructions in the peripheral circulation which, if not counteracted in the remaining peripheral circulatory pathways, must of necessity have caused eventual overfilling of the lungs despite any activity of the pulmonary vasomotors, if any such exist.

Sahli¹² criticised Welch's results adversely, giving two principal objections: (1) That in human cases of sudden œdema the pulse does not indicate paralysis of the left ventricle; and (2) that the pathological condition of the lungs is not that of congestive œdema. As to the first objection, Welch has pointed out that he had not claimed that complete paralysis of the left ventricle is necessary to the production of the result under consideration, and thinks that Sahli is in error in assuming that such a degree of paralysis is essential. A consideration of the physiological principles involved will easily prove the correctness of Welch's contention. Taking Tigerstedt's figures (and these are smaller than those given by other physiologists) for the average output at each systole of the right and left heart, 50 to 100 grams, and assuming that the

¹² Archiv f. exper. Path. und Pharm., 1885, 19.

left heart has lost one-twentieth of its working power, the result would be a retention in the left heart, and eventually in the pulmonary circulation of from 2.5 to 5 grams after each heart beat. In one minute, at a rate of 80 per minute, the amount of blood retained in the lungs would be from 200 to 400 grams. It is easy to see that the result must be a speedy overfilling of the lungs. That such a condition of affairs should take place in human disease presupposes that the vasomotor mechanisms of the peripheral circulation had for some reason become ineffective. A study of the cases in my series and others reported in the literature, shows that there is good ground for believing that such an inefficiency of the vasomotor mechanism had become established.

In answer to Sahli's second objection that the anatomical conditions of the lungs are not those of congestive œdema, Welch refers to his own microscopic studies in human cases which showed the existence of congestion, and notes that Sahli apparently relied on the pallid macroscopic appearance of the lungs, having seemingly made no microscopic examinations. Welch further states that microscopic examinations of lungs of pallid appearance often show marked hyperemia and diapedesis of red cells. I can confirm this statement from some recent studies of highly œdematous but pallid lungs after adrenalin injections. While denying the force of Sahli's contention so far as the acceptability of Welch's theory is concerned it may perhaps be true that the degree of œdema in some cases of acute pulmonary œdema of human beings is out of proportion to the degree of congestion. An increased permeability of the pulmonary vessels might perhaps be the explanation of a ready leakage of serum under conditions of but moderate overfilling of the pulmonary circulation. This point will be referred to later on.

Grossmann¹³ and Löwit¹⁴ also criticised Welch's conclusions, though there is no fundamental difference in the results of their experiments and Welch's. Grossmann caused pulmonary œdema by poisoning with muscaria, and found the left ventricle in a state of spasm with resulting venous hyperemia of the lungs. He believes these conditions contrary to what Welch had stated in his conclusions, having overlooked the fact that disproportion in the working capacity of the left and right ventricle and not loss of power in the left ventricle was the important fact. Spasm of the left ventricle (though according to Welch unlikely in human cases) could, therefore, produce the same results as loss of ventricular power. Löwit's experiments seemed to him to show that increased flow of blood into the lungs as well as diminished out-flow are two necessary conditions. If this were correct, there would be no conflict with Welch's postulates, but other experi-

¹³ Ztschr. f. klin. Med., xii.

¹⁴ Ziegler's Beiträge, xiv, 401.

menters did not find an increased flow into the lungs a necessary condition.

A study of the experiments of Welch, as well as of those who believed their results pointed to different conclusions, seems to show without question that acute pulmonary œdema may be caused by mechanical congestion of the lungs the result of disproportionate work of the right and the left ventricles. It has been mentioned before that increased permeability of the pulmonary vessels may be a subsidiary cause, and two theories regarding the development of such a condition may be mentioned. According to some authors (Bouveret, Dieulefoy, Riesman), toxic agents acting in some obscure fashion or through the vasomotor system occasion, in cases of nephritis, rapid œdema of the lungs somewhat in the same way as œdema of the glottis occurs in the same disease. So far as the vasomotor system is concerned, it is important to observe that physiologists are practically unanimous in denying the existence of such a mechanism in the pulmonary circulation. If any exists, its range of action is extremely limited and is certainly too restricted to permit of its having more than a subsidiary place in the etiology of pulmonary congestion or œdema. So far as the second possibility, that of some direct toxic increase of vascular permeability, is concerned, analogies drawn from studies of œdema in other parts of the body make it probable that such a factor is of some importance. The fact that the lung is in a measure an excretory organ, and possibly liable to injury when vicarious excretion takes place, must be considered as having weight.

Hewlett¹⁵ quotes his colleague Martin in confirmation of his belief that protein fluid of the concentration seen in one of his cases (total solids, 6.72 per cent., of which 6.302 per cent. was protein and 0.418 per cent. salts) could not have been forced through the vessel walls by any pressure short of one likely to cause actual rupture of the walls. However the facts may be as to this case, direct experiments have sufficiently demonstrated the possibility of œdema mechanical in nature to the extent that any cause save the mechanical element was a negligible factor. This does not obviate the possibility that some injurious agent acting upon the vascular permeability may be a subsidiary factor in cases of spontaneous œdema in man.

This is in conformity with Leber's¹⁶ experiment, in which it was shown that the cornea with an intact epithelium of the membrane of Descemet will stand a pressure of 200 mm. of mercury, whereas once that epithelium is removed, solutions readily filter through. Very similarly, Tigerstedt and Santesson¹⁷ found that the freshly

¹⁵ Intercolonial Med. Jour. Australasia, 1908, viii, 611.

¹⁶ Archiv f. Ophthal., 1873, xix, 125.

¹⁷ Bighang. till K. Svensk. Vet. Akad. Stockholm, 1886, xi, No. 2.

removed lung of a frog, filled with 0.6 per cent. NaCl solution will stand a pressure of 14 mm. of mercury for several hours without any escape of the contained fluid, whereas the same lung killed by slight heat or by pouring in distilled water, or frog's bile, at once allows filtration.

In view of these facts, it may be accepted as probable that some increase of vascular permeability may be a subsidiary cause in cases of recurring pulmonary Œdema, but it would seem unlikely that such a state of affairs could develop suddenly and as suddenly subside. A more reasonable view is that a temporary pulmonary engorgement acting in conjunction with an increased or established vascular permeability is the important cause.

The facts that have brought me to the conclusion that the mechanical element is predominant are the following: (1) Welch and others have demonstrated that sudden inadequacy of the left ventricle may in a purely mechanical fashion occasion acute pulmonary Œdema by causing pulmonary congestion; (2) cases of recurring Œdema have generally been cases in which there have been persistent high arterial pressure and increasing myocardial weakness; (3) the attacks are sudden in onset and usually of relatively short duration, following excitement in many instances and usually occurring at night; and (4) renal disease or other ascertainable sources of toxemia may be wanting in some cases.

The first of the points has been sufficiently discussed. As to the second, I wish to add that in the majority of cases under my own observation there has been a continuous high pressure, sometimes excessively high, and prior to the onset of the paroxysms of Œdema evidence of failure of the left ventricle. Among these evidences may be noted some increase in the size of the heart (dilatation) and weakening of the apex impulse and heart sounds, cardiac irritability indicated by extrasystoles, and oppression or anginoid attacks. Later, sometimes as a result of fatigue or excitement, an attack of acute Œdema of the lungs occurred, and following this repeated paroxysms at irregular intervals. In the cases in which excitement or effort preceded the attacks there has been primarily a violent paroxysm of palpitation, then weaker action of the heart and Œdema of the lungs. This sequence of events was clearly distinguishable in several attacks I have witnessed. These events may be interpreted as indicating a sudden extra strain imposed upon a heart struggling for a long time against excessive peripheral pressure and deprived of the protection of an intact vasomotor mechanism. Sudden external stress in normal individuals is neutralized by the inherent reserve power of the ventricle and the capacity of the peripheral vasomotor mechanism to open the external vascular channels. In cases of long-standing high pressure, arterial disease, and myocardial weakness, the cardiac power is deficient and the vessels are incapable of prompt

dilatation. Another explanation is possible in some cases, that is, that inadequacy of the coronary circulation may occasion sudden insufficiency of the heart muscle under physical strain or at times of naturally lowered cardiac power, as during sleep, without the coöperative effect of high pressure and failure of the peripheral vasomotor mechanism. Romberg¹⁸ refers to such a condition of affairs in discussing attacks of cardiac asthma which he does not distinguish fundamentally from those of recurring pulmonary oedema. It is unnecessary to enter very fully into the question of such a distinction here, but I wish to state my entire agreement with Romberg's view. It is impossible to draw a sharp line of demarcation between cases of cardiac asthma and those of acute pulmonary oedema. Few of the former are unattended with oedema of some degree, and none of the latter are free of dyspnoea of the same type as occurs in typical cardiac asthma. The difference is one of degree only, and attacks of the two sorts may alternate in the same case.

Regarding the symptoms and etiology of cardiac asthma, Romberg states: "The cause of asthmatic attacks is generally a sudden weakness of the left ventricle, which causes intense congestion of the lungs and thus leads to extreme dyspnoea. The ventricular weakness is indicated also by marked rapidity, softness, and smallness of the pulse and frequently by irregularity and in the occasional development of dilatation of the heart. The congestion of the lungs is frequently followed by the exudation of oedematous fluid into the alveoli. This pulmonary oedema, which is indicated by small and large moist rales scattered over small or considerable areas of the lung, is a further occasion for dyspnoea. The patient often coughs up oedematous fluid which may be light or dark red or even brownish from admixture of blood and may be of considerable amounts in some cases.

"The sudden loss of power in one of the sections of the heart may be occasioned by sudden embolic occlusion of one of the large branches of the coronary artery, but is practically only met with in cases of coronary sclerosis or in cases of widespread cardiosclerosis involving the distribution of blood to numerous capillaries, even though this interference be of but a moderate grade. One may, perhaps, conceive of the attacks as due to the following condition of affairs: When the power of the heart fails or when, as a consequence of overexertion or during rest as in deep sleep, the tension in the coronary arteries falls below a certain point, the existence of sclerosis of the coronary vessels may occasion an inadequate supply of blood to the cardiac capillaries, as a result of which there must be great loss of muscular power."

While I cannot subscribe to this statement in all particulars, and especially to the view that attacks of cardiac asthma or acute pul-

¹⁸ *Krankheiten des Herzens*, second edition, p. 82.

monary œdema are in the great majority of cases due to coronary sclerosis or cardiosclerosis affecting the cardiac vessels, the effect of exertion, exhaustion, and deep sleep on cardiac power seems to me undoubtedly of prime importance in the determination of attacks of acute pulmonary edema in those predisposed to such paroxysms by long-existing high arterial tension and myocardial weakness. Romberg's statements, however, indicate another possible source of such attacks in cases in which high peripheral tension has not necessarily been a predisposing factor.

In attempting to reach some conclusion as to the relative importance of toxic increase of permeability of the pulmonary blood vessels and of mechanical engorgement of the lungs resulting from deficiency of the left ventricle, I am especially impressed by the features of such cases as Case II of my series. In this case a woman with uncomplicated mitral stenosis and without evidences of renal disease has on a number of occasions during a period of ten or more years suffered attacks of sudden pulmonary œdema, most of these attacks having followed some emotional excitement. There was never any acute illness before the seizure, and the recovery on all occasions has been so speedy and complete that within twelve hours all signs have vanished. The closest inquiry has failed to indicate even the possibility of a gastro-intestinal toxemia from dietary indiscretions. The mechanical element alone remains in evidence. One could, of course, conceive of vasomotor influences if there were sufficient grounds for believing that an active vasomotor mechanism is present in the pulmonary circulation. In other cases in which a renal lesion existed, and in which on this account toxic influences require greater consideration, the rapid onset and subsidence of the pulmonary œdema are strongly opposed to the assumption that increased permeability of the vessels as a result of toxemia is a prime factor in determining the rapidly appearing and disappearing pulmonary lesion. On the other hand, a temporary weakening, under mechanical stress, excitement, or other influences, of the left ventricle, followed by restoration of equality of action of the two ventricles, could readily account for the event. The conclusion which I have reached is that the conditions outlined by Welch in his original paper are the important ones in cases of recurrent or paroxysmal œdema of the lungs.

TREATMENT. The prompt effect of a hypodermic injection of morphine in cases of cardiac asthma led me to use the same remedy in one of the earliest cases of paroxysmal pulmonary œdema that fell under my notice. The result was so striking that I have since pursued the same plan, and have found this so satisfactory that it has never thus far been necessary to employ any other remedy except as an adjuvant. Some of the cases in the present series had large numbers of attacks, and eventually died, but there never was any difficulty in controlling the attacks themselves with mor-

phine alone or supplemented with other less important drugs. When the fatal termination occurred, it usually resulted from gradually increasing failure of cardiac compensation, as in Case I. In some of my cases atropine was combined with the morphine in the hypodermic injections, but on repeated occasions morphine alone was used to test the matter and was found quite as efficient as with the addition. Therapeutists have uniformly recommended atropine to cause a drying of œdematous conditions of the lung, and the drug has, therefore, suggested itself, although it is difficult to appreciate in what manner such an effect could be brought about. When it was used independently of morphine, I found that its effects were not striking, as, for example, in one of the cases in this series in which large doses of atropine were administered during the first attack and the duration of the seizure was eight hours. In a number of subsequent attacks of apparently equal severity, a single injection, or at most two injections of morphine, with small amounts of atropine, sufficed to break up the seizures within an hour. In a few instances it seemed to me that the injections of morphine with the addition of small amounts of atropine acted more satisfactorily than injections of morphine alone, but I have come to the very positive conclusion that the atropine is of very secondary importance, notwithstanding the fact that in the discussion of Riesman's paper by the Association of American Physicians¹⁹ a number of those who took part spoke most favorably of this remedy, none, however, making any detailed reference to cases. The impression I gathered was that the remarks made were more or less off-hand and based upon the traditional applicability of this drug.

Among the few authors who have mentioned morphine as a remedy for cases of paroxysmal œdema, the most enthusiastic is Hewlett, whose experiences coincide exactly with my own. In one of his cases he used morphine followed by atropine, but found that the latter had no noticeable effect. In eight remaining attacks in the same patient he used morphine alone, and found the patient invariably comfortable and out of danger in from one-half to three-quarters of an hour. In another of his cases, during his absence, a medical colleague was called in and employed various restorative measures with little effect. Upon Hewlett's arrival, three hours after the onset, he immediately injected one-quarter grain of morphine, and within a half hour the patient was comfortable, quiet, and of good color.

The manner of action of morphine in these cases cannot perhaps be fully explained. There is undoubtedly in many of the patients an element of shock and mental disturbance which contributes to the severity of the symptoms and which may be mitigated by

¹⁹ Trans. Assoc. Amer. Phys., 1906, xxi, 170.

the injection of morphine. This view was expressed by Billings in the discussion of Riesman's paper. My experiences, however, in the treatment of many attacks in a number of patients leads me to doubt whether this explanation suffices for the very striking results obtained. If one may draw conclusions from cases of cardiac asthma in which the results of injections of morphine, with or without atropine, are so well known, and in which an element of bronchial spasm seems to exist, one may perhaps suspect that, though it is not so apparent, a similar condition of muscular spasm is also present in the cases of pure œdema, and that by relief of this, improvement is initiated. This might readily enough explain the cessation of active dyspnœa, but could not so well explain the rapid disappearance of the œdema itself. Having regard to the pathogenesis of paroxysmal pulmonary œdema and especially its probable dependence upon relative weakness of the left ventricle, the explanation of the value of morphine may be that it exercises a direct effect upon the heart itself, quieting and steadying it; and also may have a beneficial influence by quieting restlessness and relieving muscular spasm of the extremities which increase the flow of venous blood to the right heart and thus occasion a larger supply to the pulmonary circulation. It must be confessed, however, that no explanation that can be offered at present seems entirely adequate, and the value of the remedy must rest very largely upon clinical experience. A few experiments which I have made seem to confirm this. In these experiments I injected adrenalin solution into the ear vein of rabbits, causing pulmonary œdema within a few minutes. In some of the animals, injections of morphine were made immediately after the adrenalin and in others a similar injection of atropine was made following the adrenalin. In the cases in which morphine followed the adrenalin the onset of the œdema was delayed and its intensity decidedly less, though the animals eventually developed œdema and died. In the cases in which atropine was used there was an immediate onset of œdema, which was much more decided than in the cases in which adrenalin alone was used.

Chloroform was used by Lissaman in his remarkable case in which seventy-two distinct attacks occurred. He found that he could control each of these in a very short time by inhalations of chloroform, finding that within ten to thirty minutes the patient became comfortable and was soon completely relieved. The effect of his treatment adds some confirmation to the opinion that the usefulness of morphine lies in its quieting effects. So far as the use of chloroform as a routine measure in such cases is concerned, it seems hardly likely that practitioners will generally be tempted to employ this remedy. The possible dangers of this drug in cardiac disease are too apparent to require further discussion.

Nitroglycerin has been frequently employed, and upon theo-

retical considerations may be regarded as indicated. If the pulmonary œdema is the result of a partial or considerable failure of the left ventricle, vasodilatation under the influence of nitroglycerin would undoubtedly prove useful by rendering the residual ventricular power more efficacious. In cases of cardiac asthma with moderate pulmonary œdema this result is not infrequently observed, but in the more serious cases of paroxysmal œdema my experience has been that nitroglycerin and the nitrites generally fail entirely. Possibly the explanation hinted at before may explain this failure, viz., that paroxysmal œdema occurs in cases of persistent high pressure and arteriosclerosis in which the vasomotor mechanism has been exhausted to the extent that vasodilatation, under the influence of drugs or as a result of natural reflex agencies when stress is brought to bear upon the left ventricle, has ceased to be available.

Venesection has been highly lauded, and naturally suggests itself when one observes a case of severe œdema with peripheral cyanosis. Merklen and Riesman advocate this plan of treatment above all others. Abstraction of blood from the venous system may undoubtedly relieve the pulmonary engorgement by diminishing the amount of blood flowing toward the right heart, and very probably it is in this manner that its usefulness is explainable. Compared to the simplicity of a hypodermic injection of morphine, venesection is a procedure of considerable gravity, and its effect cannot be more prompt or satisfactory.

After the first stage of the attack has been controlled by an injection of morphine and atropine, it is desirable to make use of cardiac stimulants to revive the power of the left ventricle and to promote vasodilatation, if this be possible. For these purposes injections of strychnine, digitalin, and nitroglycerin may be employed, and aromatic spirit of ammonia or brandy may be given by the mouth if the patient is able to swallow.

The after-treatment in cases in which one or more attacks have occurred consists in strict regulation of the daily life of the patient to avoid fatigue, excitement, cold, and physical strains, and some care of the diet so as to prevent overloading of the stomach and superalimentation, particularly at the evening meal. Renal cases may require warm or hot baths and particular care of the diet, and when myocardial weakness is evident after attacks, moderate cardiac stimulation may with advantage be used more or less continuously. On account of its action on the coronary circulation and on the kidneys, caffeine is a drug that may be particularly useful at this time; but strophanthus, digitalis, or nitroglycerin may be desirable.

In some of the cases under my care who had the constant attendance of a nurse I have left directions for (1) the immediate administration of aromatic spirit of ammonia upon the first suggestion of an attack, to be followed by (2) an injection of morphine

sulphate, $\frac{1}{4}$ grain, with atropine sulphate, $\frac{1}{250}$ grain, when the first definite symptoms appeared; and (3) the subsequent repetition of morphine and atropine after fifteen minutes and later injections of strychnine and nitroglycerin. This plan served to control many threatening paroxysms before they had time to become severe.

THE CONTROL AND TREATMENT OF HYPERTENSION AND ARTERIOSCLEROSIS.

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THERE are a number of underlying facts which the diagnostician and the therapist must continue to bear in mind if he would successfully prevent the results of hypertension and influence the onward march of existing arteriosclerosis. To these facts I wish to allude.

Cardiovascular, more particularly arterial changes furnish the fundamental morbid processes in the largest number of deaths after the fortieth year. We are surprised when we examine our clinical material, more particularly that seen in private and consultation practice, to note the recent enormous increase of cardiovascular disease. We are promptly forced to the conclusion when this is compared with hospital statistics that there is an increase of the diseases of the arterial tree, coronary arteries, the myocardium, and in the nerve supply of the heart, the farther we are separated from hospital practice.

A careful study of the last 3200 cases of internal disease seen in private and consultation practice offers food for reflection. These include:

Arteriosclerosis	276
Endocarditis	135
Angina pectoris	44
Hypertension	67
Mitral obstruction	62
Aortic obstruction, vascular, endocardial (inflammatory)	151
Mitral insufficiency	267
Aortic insufficiency	20
Myocardial degeneration	277
Heart hypertrophy	63
Heart dilatation	59
Senile hearts	25

In a long-hand written report of the lectures of Benjamin Rush, which has recently fallen into my possession, that erudite clinician of enormous experience and supposed unlimited clinical material, makes the statement that in all of his experience he had seen but

one case of angina pectoris, and he mentions the name of another physician practicing in Philadelphia who had also seen but one case.

Taking our clinical material into consideration, we are forced to the conclusion that hurry, worry, and excesses are at the bottom of a large majority of our cases in which we have degenerative changes in the cardiovascular system following a long or short period of hypertension. That heredity plays an important role in many of our cases we cannot deny, but we are equally positive that if these patients who are burdened with this unfortunate tendency were cautiously watched and correctly advised by the physician, changes of a degenerative nature in the heart and bloodvessels might be longer postponed. This is particularly true of arteriosclerosis as it affects the coronary and cerebral bloodvessels. It is not uncommon for us to get the history of three or four cases of coronary disease in one family, and we have family histories in which as many members of a family have died, either of cerebral apoplexy or of other brain disease associated with vascular anomalies.

These positive facts teach a valuable lesson. The study of the family history is too much neglected. Men who do not keep records, who do not question patients systematically, are very likely to overlook entirely the valuable facts which are gained by a thorough study of the patient's antecedents. These may seem rather commonplace remarks, but the consultant is so frequently brought face to face with these facts and understands so thoroughly their great importance that the opportunity to present them ought not to be neglected.

Modern pathology makes clear beyond peradventure the further fact that there is a physiological hyperplasia invading the intima during early life. We are forced to consider the separate artery as an organ, therefore, a part of the body which has positive functions to perform; that its task is not single but multiple, and that the performance of its daily undisturbed work is attended even during the earliest years of life with a compensatory deposit for the preservation of these organs and the continuity of the circulation. As soon as this physiological hyperplastic change of the intima because of age, overwork, strain, toxemia, or from any other causes is forced into a stage of hypertrophy, we have the beginning of arteriosclerosis.

There is a considerable period of hypertension which precedes this profound change in the arterial tree which, however, in the majority of cases is not recognized, because of a natural tolerance; and when present there is almost immediate compensation. If hypertension persists unrelieved and the factors which continue it remain uncontrolled, organic changes in vital organs are usually present, particularly in the heart, kidneys, and within the splanchnic area, before the patient presents subjective manifestations. In other cases, however, rather limited changes during the early days

of arteriosclerosis are sufficient to cause alarming symptoms and not infrequently prompt death. Thus, there may be early in the history of atheroma or arteriosclerosis only a small lime plaque close to the mouth of a coronary artery but of sufficient size to choke the heart without a second's warning by covering its mouth.

Hypertension long-continued is the leading cause of arterial degeneration. It must be remembered, however, that arteriosclerosis once established, hypertension is not a necessary feature; arteriosclerosis may be present for years with normal, subnormal, or high blood pressure. Hypertension upon which we fail to make a favorable impression by rational treatment is already associated with changes in the kidneys, heart, or the splanchnic area. We have failed to recognize the enormous extent of the splanchnics and their importance as pathogenical factors in the causation of hypertension and distant cardiovascular disease. The Germans have recently said, "happy is he whose splanchnics are normal and are offering no resistance to the circulation."

To prevent the baneful organic changes following hypertension we must recognize its presence early. Modern methods make this easy. Why not take advantage of these methods as we do of those which unearth kidney changes? To know exactly what resistance the heart has to overcome in the periphery is more important than to recognize the presence of albuminuria.

In considering the subject of hypertension we must remember the great clinical significance of the tightening and relaxation of the arteries of the body, the urgent need of separating the "two factors of the vessel wall and the contained blood."

Why not educate the masses in this direction that the majority may escape the ravages of final degenerative processes? When the ravages of time force the individual to seek the oculist because of changes in the crystalline lens, and this organ is flattening, and glasses are needed to compensate, or they need to be changed for this retrograde process, he has become a fit subject for blood pressure study. He is most likely in a period in which prophylaxis is demanded and it will often lead to satisfactory results. When changes are found in distant organs it must be remembered that hypertension or slightly increased blood pressure may prove an equalizer, compensatory, and ought not to be disturbed. The sphygmomanometer has proved itself a very valuable adjunct in diagnosis. It is easily and frequently misinterpreted and abused. No man should reach conclusions from the study of systolic pressure alone; if he would base treatment upon a firm basis he must think clearly, brace himself against one-sided reasoning, and give proper values to all data which are unearthed by the thorough consideration of subjective symptoms and the knowledge gained by physical examination: the sphygmomanometer furnishes but one strong link.

When we find with evidences of hypertension or already present arteriosclerosis accentuation of the aortic second sound we know that "the door is being slammed"—the cusps forming the door—that there is a peripheral obstruction which heart and artery are trying to overcome and we must act accordingly.

The point which I seek to impress with greatest earnestness is that if we would prevent arteriosclerosis we must consider the artery an organ with a capacity which is great for work, but which when abused or overworked, insulted or poisoned, revolts and begins to degenerate. When one robs the heart of its sleep he is damaging that organ and the entire vascular system. Lauder Brunton in his happy way has recently said, "the heart practically sleeps more than the brain or the body, but the great distinction between the sleep of the heart and that of the brain, is that the sleep is so short at a time." The heart and arteries demand thirteen hours of this sleep daily (this statement surprises those who have not computed the time). When robbed of this repose the periods of rest are shortened; cardiovascular organs are forced to work over-time, more rapidly than before, and the foundation for retrograde process is laid. Nature will bear insult a reasonable time; the revolt will come sooner or later with unfailing certainty.

The final break in a large number of cases includes myocardial degeneration with all of its pangs. Hypertension and arteriosclerosis are increased less by the routine work of the day than by the innumerable outside affairs and engagements which occupy so much of the time of the busy man (particularly the physician), and cut his rest to a minimum. These workers hold the string taut, the tension under which they work is enormous; their bearings are worn, until at last the string snaps and we are called to repair and reconstruct—often when it is too late.

Hypertension will often lead to a strong suspicion of renal invasion. This is true when associated with hypertrophy of the left ventricle though albumin be absent from the urine during a long period. The renal arteries may be far advanced in arteriosclerosis without invasion of other kidney structures which when changed add casts and albumin to the urine. From the careful investigation of the diseases of the ductless glands we are convinced that these have a marked influence in producing arterial change and that in considering the rational treatment of hypertension we are not to divorce ourselves from this possibility. The production of arteriosclerosis in animals by the injection of adrenalin is proof positive of the correctness of this statement and must have a decided bearing on the dietetics of hypertension and arteriosclerosis. The younger the subject the more unfavorably does he react to hypertension and arteriosclerosis. Indeed, we are often justified in speaking of the presence of arteriosclerosis in the aged as a protective process—a true paradox. If we would successfully control blood pressure

we must have the hearty coöperation of the patient. He must be willing to surrender himself absolutely to his physician. Carlye's definition of genius included infinite attention to detail. Every possible bearing of the life and habits of the individual upon these destructive and degenerative processes must be taken into account by the therapist, and this in detail.

Romberg says, "Everyone acquires his arteriosclerosis within the circuit which he has taxed most." Upon this truth we are to act, particularly in attending early to local disturbances, to all intestinal anomalies, including chronic constipation, intestinal indigestion, and the dyspepsias. Even a distant irritation as a urethral stricture or unrelieved prostatic hypertrophy may keep up hypertension and lead to arteriosclerosis.

Tobacco, that is, nicotine influences blood pressure very powerfully. Lauder Brunton says, "The rise of blood pressure is so great that I have never seen it equaled after the injection of any drug, with the exception of suprarenal extract. This rise is due to contraction of the arteries. The ultimate effect is to increase the rapidity of the heart. When this pulse is quickened no stimulation of the vagus will slow the heart, as its terminal branches in the heart are paralyzed by the drug." I continue to quote Brunton: "Usually tobacco is employed by smoking, either in the form of cigars or cigarettes, or in a pipe. When used in any one of these forms it is not pure nicotine which reaches the mouth, but really the products of the dry distillation of tobacco, containing a large quantity of pyridine and picoline bases. Probably nicotine in greater or less quantity is also present. The proportions of the pyridine and the picoline bases in the tobacco smoke vary according to the mode in which it is burnt. In a cigar there is freer access of air, so that much collodine and little pyridine are formed, while in a pipe much more pyridine is produced, and thus stronger tobacco can be smoked in a cigar than in a pipe. So much is this the case, that tobacco which in the form of a cigar would produce no disagreeable effect, may cause giddiness and vomiting if smoked in a pipe. The smoke from a pipe or cigar usually passes simply into the mouth and out again, either through the mouth or the nostrils; but when smoked in a huka or narghileh, the smoke is inhaled into the lungs, and this is frequently done also by people who smoke cigarettes. When a huka or a narghileh is used, the smoke passes through water before being inhaled, and it is thus deprived of most of its poisonous constituents; but this is not so with the smoke of cigarettes, and, as absorption occurs very rapidly from the pulmonary mucous membrane, cigarette smoking is sometimes very injurious. There is another reason, however, why cigarette smoking is frequently more harmful than smoking a pipe or cigar, and it is that cigarettes are small and can be smoked in a few minutes, so that many more cigarettes than

pipes or cigars are consumed in the course of a day, and the total quantity of tobacco used is thus much greater in the form of cigarettes. Smoking in moderation does not seem to be injurious to grown-up people, but there appears to be a general consensus of opinion that it is very distinctly harmful to growing lads." Whatever conclusions we reach concerning the advantages or pleasures derived from tobacco by the healthy individual, it should be absolutely interdicted in the presence of hypertension and arteriosclerosis.

Coffee raises blood pressure because of the caffeine which it holds, and this rise is associated with increased rapidity of the heart's action. It makes the heart irritable, it increases the power of the heart's contractions, it places an extra load upon the kidneys, increasing the urine flow, and the solids of the urine are increased by overtaxing its secreting cells. Because of these effects I have for some time held that men beyond fifty who get insufficient exercise or are brain workers, and children before puberty, cannot with safety to themselves drink coffee. There is something in the coffee bean besides the caffeine, of which it can be freed, which also acts as a healthful stimulant to brain and other organs and makes it a valuable article of diet. A patented process is now being used in Germany by which the coffee bean is freed of 90 per cent. of its caffeine. This coffee has been largely used abroad during the past two years with great satisfaction. There is scarcely a health resort in Germany which is not largely substituting this coffee for the ordinary coffee of commerce. The taste of the coffee is not materially changed from that of ordinary coffee, the effect, however, upon the heart and bloodvessels is decidedly different. Patients who have never been able to take coffee, whose circulation, particularly the heart, has been unfavorably affected are able to take it when freed of its caffeine with impunity. During the past year I have given it a fair trial and am thoroughly convinced of its value and the desirability of using it in all cases of hypertension, arteriosclerosis, and irritable heart; indeed, I believe that it is the ideal coffee for all brain workers or those of sedentary habits after the age of fifty. Blood pressure is not increased by its use, nor is there palpitation, or annoying systolic force.

The dietetic treatment of hypertension and arteriosclerosis is most important. No abnormalities from which we suffer are more favorably influenced by rational diet than are these conditions. The surcharged artery is always a menace to the individual. When the pabulum which it carries contains an excess of purin bodies, or of irritating substances of any kind, hypertension is increased and arteriosclerosis invited.

We have often been surprised by the routine and empiric methods which are practised in many sanatoriums, here and abroad. In some of these, patients with hypertension are treated by what is known as the "flushing method." It is supposed that by giving quarts

of water daily the noxious substances which are floating in the blood are promptly eliminated. No thought is given to the distention of vessels or to the extra work given the heart and kidneys which follows this irrational treatment. Healthy elimination must, of course, be invited but not at the loss of heart strength, nor by the overdistention of the artery or the overworking of the kidney. No physician who prefers the use of natural methods decries the influence of pure water, but we must raise our voices against its excessive and empiric use.

In connection with the subject of diet we are again reminded of the overpowering importance of the study of the individual case. The tolerance of these patients must be tested before full directions can be given. In some we find a low carbohydrate tolerance, in others, purin bodies at once choke the furnace, in still others the digestive organs are so changed as to influence unfavorably the vascular system because of motor insufficiencies, either in the stomach or the intestines. In other cases we find that an ordinary diet is keeping up a hyperacid state which promptly leads to a train of symptoms including joint changes, final gout, with associated cardiovascular disturbances. Modern methods make it possible for us to clear the horizon without great loss of time, but with great benefit to the patient.

Sufficiently reliable results for practice are obtained from the estimation of the purin bodies by the Walker-Hall apparatus, the uric acid output after the method of Rehmann, while the tests for indican, ammonia and other noxious substances are easily made by those who care to study these conditions thoroughly.

Patients with hypertension or arteriosclerosis demand continuous watching; articles of food may be tolerated at one time which for unknown reasons exaggerate symptoms and are harmful at other times. If we had our choice of treating angina pectoris or coronary disease by a single method I think we would all promptly choose the dietetic. It is surprising to note how much can be accomplished even with advanced sclerosis of the coronaries by a rational diet and proper living without the administration of a single grain of medicine. I know of no disease in which the results are so brilliant following appropriate diet as in angina pectoris. Patients who have had repeated severe seizures, who suffer from stenocardia on slight exertion, promptly yield to the diet which gives them just food enough and not too much, which withholds from them the heavier and more indigestible articles of diet, who take but little meat, never more than once daily, often for days no meat at all; but who are preferably given eggs, fresh fish, easily digestible vegetables, and a limited supply of liquids. These patients demand the minimum of food that will nourish them. Many patients with angina pectoris have promptly lost their lives because of a single dietetic indiscretion. I cannot express too

forcibly my ideas on this subject in connection with this disease which has robbed us of so many brilliant colleagues. The question of diet is of the greatest importance in connection with those cases in which there is a strong hereditary tendency.

Agreeable occupation which favors a quiet mental state is of enormous value in the treatment of both hypertension and arteriosclerosis. An exalted and overwrought brain must of necessity be associated with the tear which follows the abuse of that organ. This is, at once, associated with hypertension; prolong it and the associated pathological conditions will not be long postponed. I have recently had an example in a lawyer who was engaged in the promotion of an enterprise of enormous proportions, who was without hereditary taint, in whom the hurry, worry, and excitement, associated with the launching of this project promptly led to enormous hypertension, even thickening of the arteries, renal invasion, and death in the course of a few months. These cases are not uncommon, and while the process is not always so rapid or widespread as in the case mentioned, subjective and objective symptoms are not long postponed.

Therefore, to the busy brain worker, whether he has hypertension or not, we are forced to recommend periods of quiet, prolonged rest, change of scene, proper exercise, and temperance in all things. While alcohol may not directly cause arteriosclerosis we are very sure that it does so indirectly and that productive changes in the kidneys and other organs consequent upon its use calls upon the cardiovascular system for extra work which finally leads to change of a degenerative character. Individuals react differently to the social glass of wine or liquor. My experience has been that alcohol in any form is injurious in all cases of hypertension and arteriosclerosis except in a final stage associated with myocardial weakness and broken compensation, to which I shall again refer.

We are all praying for the prolongation of life which is to follow the introducing of the lactic acid bacillus as suggested by Metchnikoff. To those of us who have turned the corner at fifty there is cold comfort in the statement of Metchnikoff that if our lives are to be prolonged we should have taken advantage of the inhibitory action of the lactic acid bacillus during our early days. However, buttermilk is on trial as never before. Whether by suggestion or by its inhibitory action on toxin producers in the intestines, it has seemed to make light the hearts of many.

The baneful effect of excessive coitus has not been thoroughly recognized by the profession. At any rate, the hypertensive and arteriosclerotic have not been sufficiently warned against excessive indulgence. In some of our cases abstinence becomes imperative. This is particularly true of those types of vascular disease associated with arterial spasm.

We forget that the heart muscle is not the only true muscle con-

cerned in the circulation of the blood. The skeletal muscles are as much a part of the circulatory system as are the capillaries, the veins, or the lymphatics. A healthy circulation demands the assistance which it receives from the heart muscle, the arteries, capillaries, veins, lymphatics, and not the least important, the skeletal muscles. The circulatory poise is best preserved by attention to all of these separate organs. The healthy stimulation of muscle by massage, proper exercise, with sufficient periods of rest, becomes exceedingly important in the treatment of the conditions which I am considering. Cases in which active exercise is out of the question demand passive movements. The Zander movements are particularly useful. It is unfortunate that we have in this country no such institutions as we find in Germany, rivalling each other, in which it is possible by means of the Zander apparatus to stimulate most muscles of the body and to do this without danger to the heart or bloodvessels.

The introduction into therapeutics of the various devices perfected by Zander marked an epoch in mechanotherapy which has not been sufficiently appreciated by the profession. In practice many well-selected cases of hypertension and arteriosclerosis are favorably influenced by warm and hot baths. I have observed the effect of these at Nauheim, Weisbaden, and Karlsbad, and make the statement knowingly that in well-selected cases, though the practice is empiric, the results are often reassuring.

No one health resort has a monopoly of hot carbonated or saline water. On the other hand, we cannot ignore the fact that the environment of success is not to be disregarded. The rest, change of scene, and divorce from active life are unquestionably factors which make it possible to give the heart, arteries, and other organs that rest which is so much needed in these cases. If the patient will yield, is willing to rest at home, the Nauheim baths with resisted movements are often used to better advantage under his own roof than in the crowded hotels or boarding houses of the health resort, or in the depressing atmosphere of seriously sick patients. The discouraging factors with busy men are that they fail to take advantage of our suggestions; do not rest absolutely, and continue the supervision of their interests from their homes, which often complicates matters and brings home treatment into disrepute.

Until within the past year I failed to recognize the value of high frequency currents for the treatment of either hypertension or arteriosclerosis. During the past summer I had abundant occasion to note the effects of this treatment in Karlsbad under the direction of Dr. Buxbaum. Formerly I attributed the relief of subjective symptoms to the overpowering influence of suggestion. I was promptly convinced, however, that this conclusion was unjust and found that this method of treatment had influenced a large number of cases favorably, that blood pressure was reduced, and

that subjective symptoms were relieved; in some of the cases the relief continued during a number of months after a sufficient period of treatment.

We are not to conclude that this is a curative agent. It does, however, materially influence blood pressure, and it does dissipate in many of these cases, the annoying subjective symptoms. In advanced arteriosclerosis, the blood pressure is not likely to be reduced. In some the pressure may be raised by the treatment. The cases which react favorably are young subjects with hypertension or those who have symptoms of incipient sclerosis; in these there is a lowering of blood pressure with corresponding improvement in the general condition. Laquer holds that in these cases the benefit is gradual but, as a rule, permanent. He also holds that when there is cardiac disease without arteriosclerosis, good results are obtained by the local application of one electrode over the precordial region. How this agent acts I do not know; that it is beneficial I am positive. I have seen cases of angina pectoris treated by this method in which subjective symptoms were held under control during long periods. I do not refer to those cases with the larger attacks, but to those in which the sternal pang and oppression were present at some time during each day.

I am sometimes asked what drug have I to recommend for the relief of the conditions under consideration. Drugs alone are inadequate to meet the indications mentioned, but there are drugs which may be given in connection with the methods of treatment already suggested which lead to material benefit and which in incipient cases may lead to cure. The preparations of iodine have for years been the sheet anchor of the therapist for the treatment of arterial disease. The great trouble in the average case is that the physician in giving his original prescription for the iodide fails to make clear the urgent need of long-continued treatment with these remedies. If the iodides are to relieve or cure they must be administered during months and even years. Patients who do not tolerate the potassium iodide often benefit by alternating the use of the strontium, rubidium, and sodium salts. I have found that the strontium and rubidium salts are better borne than the sodium or potassium iodides. The more valuable iodides for the control of symptoms and the influencing of the underlying process are the potassium and sodium salts. It is very easy in the average case to establish tolerance by giving the strontium or rubidium salts first; finally the sodium salts, then a long-continued period during which the potassium salt is taken, and as time wears on a return either to the sodium or rubidium iodide for a short time. The potassium salt, of course, is to be given during the longest possible period. Recently there have been introduced other preparations which have also seemed to be efficacious, and readily borne. I refer to sajodin, tiodin, and

eustenin. The profession has had a fairly satisfactory experience with sajodin. Tiodin is a preparation of iodine and thiosinamin. In occasional cases the tiodin has served very well. Eustenin has lately been introduced and is a combination of sodium theobromate and sodium iodide. It is a whitish hygroscopic powder, soluble in water. Theobromin has been supposed to increase the coronary circulation and advances the blood flow through these vessels and through the cardiac muscle; the iodides dilate the vessels and cause a diminution of the viscosity of the blood. The combination of the iodine and theobromin in the form of eustenin has in some cases in Van Noorden's and Jargie's practice been satisfactory in relieving subjective symptoms and reducing blood pressure. A number of years ago, Huchard recommended the use of pure theobromin for the relief of sensory symptoms associated with coronary sclerosis. This drug has been given a fair trial; the majority of those who have used it are willing to confirm Huchard's observations. Theobromin is particularly useful in cases of angina pectoris, and intermittent claudication or painful vascular spasms. I have been in the habit of prescribing not more than 0.24 gram of pure theobromin every morning and night in the average case. It is a purin body and ought not to be used in too large doses. In practice I have found that larger doses are likely to cause annoying headaches. Cases in which with myocardial weakness and coronary sclerosis there are almost continuous sensory symptoms are likely to show improvement from the frequent administration of small doses of the drug; 0.12 gram may be given every two or three hours according to the urgency of the symptoms. The salicylate of theobromin in my experience is not as efficacious as is pure theobromin. Painful processes due to sclerosis, associated with myocardial degeneration, broken compensation, dropsies, in spite of the thickened arteries frequently show wonderful improvement after the administration of powdered digitalis in 0.1 gram doses with 0.6 gram of the salicylate of theobromin. I have occasionally substituted for the latter 0.24 of caffeine sodium salicylate. In these cases it is wise to combine with the digitalis treatment the daily morning administration of one tablespoonful of a saturated solution of Rochelle salts or magnesium sulphate in one-half gobletful of hot water before breakfast. This will empty the splanchnics and act as a safety valve. In these cases because of extreme weakness an occasional glass of claret, Tokay, or even a small dose of whisky, or ethereal stimulant, preferably the ethereal tincture of valerian, will brace the patient and carry him over a critical period until the other remedies already suggested come to his rescue.

Persistent hypertension treated with the diet and methods of living suggested is often favorably influenced by the administration

of the Lauder Brunton draught; the modified prescription for which I offer:

R—Sodii nitritis	3.0
Sodii bicarbonatis, C. P.	32.0
Kalii nitratis	32.0
Aquæ	q. s. ad. 132.0—M.

Sig.—Shake well. One teaspoonful in a gobletful of hot water before breakfast.

In rebellious cases of hypertension, usually associated with sclerosis, I give this remedy in the same dosage and in the same way before each meal. Small doses of chloral (0.3 gram) will in many cases of uncomplicated hypertension, with attention to the digestive system and thorough emptying of the intestinal tract at short intervals by means of salines and the use of alkalis, cause a decided drop of blood pressure and great relief of associated subjective symptoms.

Pounding, irritable hearts, with hypertension in which the systolic contraction is unusually strong, the area of cardiac impulse outside the nipple line, with or without vertigo, more or less discomfort referable to the head, are, as a rule, relieved by the administration during two or three weeks, three times daily, of from 1 to 1.5 gram of strontium bromide with from two to four drops of either tincture of veratrum viride or an equal dose of tincture of aconite root. The nitrites, including nitroglycerin, sodium nitrite, amyl nitrite, are most useful in those cases of arteriosclerosis associated with sensory symptoms. For the continuous treatment of hypertension I prefer the sodium nitrite with theobromin to any of the other vasodilators. For the relief of vascular spasm, attacks of angina, in which the physiological action of the nitrite needs to be prompt, nitroglycerin, erythrotetranitrate, amyl nitrite are preferable. Small doses of glonoin in extreme cases produce very little effect, only evanescent results. When we are face to face with danger in these cases only large doses of glonoin, preferably in liquid form, and not in tablets, dropped upon the tongue will produce the physiological effect which is absolutely necessary to prolong life. The lives of patients with threatening death from cardiac spasm or true stenocardia have, in my practice on several occasions, been prolonged during many years by the administration of nitroglycerin in large doses, sometimes as much as fifteen drops in a single dose.

We are not to be held by the rule which interdicts the administration of digitalis in all cases of hypertension, for occasionally, in spite of high blood pressure, there are convincing evidences of myocardial weakness without marked fibroid degeneration in which digitalis does yeoman's work. Such a case I have at present under observation; we hesitated to administer digitalis during a long period because of the serious sensory symptoms due to coronary disease, but all of these yielded promptly after the use of digitalis when the systolic strength was established.

I am fully agreed that Mackensie is correct when he makes the statement that "some of the most violent attacks of angina pectoris have occurred in people in whom the exhaustion of the heart was temporary, and the restoration of reserve force resulted in a complete cessation of pain and in permanent recovery." Some of these I have treated with small doses of strychnine and 0.3 gram doses of lactate of lime.

In the treatment of both hypertension and arteriosclerosis we receive valuable indications from the consideration of the general condition of our patients and the constitutional treatment accordingly administered. With associated renal complications and anemia the chlorides are particularly valuable. We must continue to keep before our mental vision the urgent necessity of conveying to the heart and the entire system the pabulum which it demands, including an abundance of oxygen.

The life of the Venetian Doge Cornaro who presented a discourse on "The Art of Living Long" has never ceased to interest me. It is a classic and should claim your attention. Cornaro had, I dare say, subjected himself to overwork, and possibly to many other baneful influences, in spite of which he reached his eighty-third year. He appreciated the fact that he had made many mistakes, and that he was fast nearing his end. His later experience justified the production of a series of articles, "Wherein the Author details the Method by which he Corrected his Infirm Condition and Strengthened his Naturally Weak Constitution and Thenceforth Continued in the Enjoyment of Perfect Health." He lived to be over one hundred years old, enjoying to his last day the full possession of his faculties and many other pleasures which he was quite sure he would not have enjoyed had he disobeyed the laws of Nature. A single quotation is justified: "Divine sobriety, pleasing to God, the friend of Nature, the daughter of reason, the sister of virtue, the companion of temperate living, the loving mother of human life, the true medicine both of soul and body, how much should men praise and thank thee for thy courteous gifts, for that gives them the means of preserving life in health, that blessing which it did not please God we should have a greater in this world, life and existence so naturally prized, so willingly guarded by every living man." This paragraph contains the essence of therapy which the thinking physician must apply against hypertension, whatever the cause.

THE TONIC USE OF DIGITALIS.

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THE diagnosis of the disturbances of the different functions of the heart muscle has made tremendous strides under the influence of Mackenzie's graphic method of recording the heart movements and Wenckebach's ingenious application of Gaskell and Engelman's explanations of physiological phenomena. Studies in the disorders due to disturbed conductivity have opened a new chapter in the seemingly exhausted subject of the pathology of the heart. We now interpret the alternating pulse as a sign of disturbed contractility, and the disorders of excitability and rhythmicity are rapidly becoming identified. The rational therapy of the future will have to aim at the correction of these primordial disturbances, and modern pharmacology will have to rise to the demand for the various specifics. Unfortunately, tonicity, the most important function of the heart muscle from a clinical standpoint, cannot be directly recorded or estimated. Its variations must be gauged by a study of the functional disturbances due to impaired circulation. Stretching of the muscle and distention of the ventricular cavities follow necessarily on a loss in tonicity, and the result is a retardation of the blood stream.

The influence of the tonus on the efficiency of the heart muscle may be appreciated from the following observations: It has been shown that the ventricle does not empty itself completely with each systole. It fills during diastole with a varying amount of blood, depending mainly upon the length of diastole and the strength of the forces which aspirate the blood into the heart. We know also that a muscle can do most work when it is slightly stretched. Thus, with a good tonicity, the strength of contraction of a given heart muscle will vary directly with the amount of diastolic filling of the ventricle. Also, as the capacity of the ventricle varies as the cube of the diameter, less shortening of the muscle is needed to expel a given quantity of blood from a well-filled than from a poorly-filled cavity. If, however, the stretching of the muscle be due to a loss of tonicity, even an increase in contractility cannot prevent a loss in the amount of work done. This can be shown in the laboratory by loading a muscle and stretching it beyond the limit of its tonicity. In this condition it can perform very little work.

There is still another way in which a loss of tonicity interferes with the action of the heart. Under normal conditions ventricular systole begins with an increase of tonus, which raises the pressure in

the cavities to that of the pulmonary arteries and the aorta before any shortening of the muscle has taken place. Thus, with the opening of the valves, muscular contraction begins under the most favorable conditions of tonicity and load.

These conditions are changed just as soon as any one of the heart valves begins to leak. The escape of blood allows the ventricle to change its shape at the very beginning of systole, there is no rise in tonicity, and the fibers begin to contract too soon. The contraction, which should be afterloaded, becomes isotonic, that is, the amount of work performed is practically equal throughout the duration of contraction, and much more energy is used up.

The lack of isometric contraction preceding the isotonic contraction can be overcome to a considerable extent by an increased diastolic filling of the ventricle. This stretches the muscle enough to raise the tonicity appreciably before the beginning of systole. A shorter contraction is then needed to expel the usual amount of blood. This compensatory process soon tends to become harmful, as the overstretching of the heart muscle lowers tonicity still further.

It is its influence on this vital function of tonicity which has given digitalis its unique position in the therapy of cardiac disorders. As far back as 1882, François Frank showed that digitalis strengthens the muscular rings which are largely responsible for the competency of the auriculoventricular valves. The relative mitral insufficiency seen in various conditions of depression—*anemia*, cardiac overstrain, and failing compensation—is due to a loss of tone in this ring, and can be influenced favorably by digitalis. Since Frank's publication, numerous investigators, notably Cushny and Cameron, have come to the same conclusion, and Gossage has tried to prove that this effect on tonicity constitutes the entire beneficial action of digitalis. This view, however, is probably not wholly justified. Balfour¹ says: "All the benefits we obtain from digitalis are inseparably connected with its tonic action; they flow from the power that digitalis has of increasing muscular elasticity, and the improved metabolism of all the tissues, but especially of the myocardium."

The effect of digitalis upon the heart depends upon the amount of the drug present in the body. In fully developed heart failure, with dilatation, enlargement of the liver, and *œdema*, we give digitalis in massive doses. Accumulation takes place owing to the comparatively slow excretion, and the body becomes saturated. Then appear the toxic as well as the beneficial effects of digitalis. The slower pulse and longer diastole, due to *vagus* action, permit a more complete recuperation of the contractile power, and the deep and more forceful inspirations, due to stimulating of the respiratory centre, aid in the diastolic filling of the ventricles. The dose of digitalis

¹ Clinical Lectures on Diseases of the Heart, p. 360.

must be adapted to the rate of its excretion if we want to get the effect on tonicity alone. This rate has been found by Balfour to be about 1 grain in twelve hours. Accumulation does not take place with this dose, and the drug may thus be given over periods of weeks, months, and even years without any toxic action.

This valuable point in the art of giving digitalis has received scant mention in the literature of the subject. Most of the experimental work has been done on normal animals, and with toxic doses. In this way many errors have been introduced into the clinical application of digitalis; for instance, the action on the peripheral vessels which appears only with toxic doses.

Cloetta² has made some excellent studies in this use of "tonic" doses in contradistinction to the "anti-asystolic doses" of Huchard. First, he took normal animals and gave digitalis in increasing doses for periods varying between a few months and two years. There was no change in the pulse frequency, and measuring the blood pressure during compression of the aorta showed no increase in the ability of the heart to overcome the obstruction. Autopsies showed no change in the weight or size of the heart. The result of the experiment was very different, however, when performed on animals with an aortic insufficiency produced by the Rosenbach method. The hearts of the control animals which received no medication showed an increase in weight of 47 per cent. over the normal average, while the hearts of the treated animals showed an increase of only 25 per cent. The work-output of the digitalis heart muscle was vastly greater, however, than that of the controls.

Four of the control animals died of heart failure, while none of the treated animals showed any symptoms of heart disease. The functional test—blood pressure during compression of the aorta—showed practically normal records with the treated, and much lower figures with the control animals.

We see from these experiments that the larger hypertrophy gives a poorer functional result. This can probably be explained in the following way: The loss of tone is a stimulus to hypertrophy, which, however, cannot make up entirely for the original loss. Digitalis helps the muscle to keep its tone; less hypertrophy is demanded, and the new muscle is again enabled to work more effectively.

With the great development of our modern methods of physical diagnosis, the tendency has been to rely too much on the direct examination of the heart. As stated at the beginning of this paper, we must look elsewhere for the first signs of failing tonicity, and if we wait for indications from the heart itself, we will need the massive doses to get out of danger. Neither will blood pressure determinations help us, as they offer no means of measuring accurately the systolic output of the heart. Plesch's³ procedure, which seems to be

² Archiv f. exp. Path. und Pharm., lix.

³ Ztschr. f. exp. Path. und Ther., vi.

the only one giving any degree of accuracy, is hardly applicable clinically.

Loss of tonicity shows itself first in general symptoms. In the presence of heart disease, persistent cough with rales over the basis of the lungs may be attributed to a loss of tonicity of the left ventricle. A similar condition on the right side of the heart shows itself first in the swelling of the liver, dyspeptic symptoms, and slight pitting of the ankles, which disappears over night. When these symptoms coincide with the appearance of a mitral or tricuspid murmur, all indications are present for the tonic doses of digitalis.

The tonic use of digitalis in cardiac disease is of comparatively recent introduction. The cumulative, toxic effect from repeated small doses seemed so inevitable as to prohibit any such continued medication. Traube was the first to see a way out of the difficulty, and he showed that digitalis could be used over long periods in slowly increasing dosage. A little more attention was paid to the subject when Baelz¹ reported the remarkable case of a woman who had taken an infusion of digitalis for seven years. While taking the drug she was able to work, but any attempt to stop was followed by diminution in the amount of urine, œdema, flashes of light, tinnitus aurium, and subjective heart symptoms, which would disappear within a few hours after resuming treatment. In the course of seven years she took 810 grams of digitalis.

Balfour in England, Fraentzel⁵ in Germany, and Huchard⁶ in France have been pioneers in this field.

Balfour, in his lectures, discusses the subject so fully and so well, that very little has been added since. More recently, Groedel,⁷ Naunyn,⁸ and Kussmaul⁹ have insisted on the advantages of this method. Kussmaul has given us, in his usual classic style, a most complete and accurate account of a case in which autopsy showed the following conditions: Generally dilated heart, stenosis and insufficiency of the aortic valves, aneurysm of the aorta, arteriosclerosis and endarteritis of the coronaries, and contracted kidneys. He first took digitalis in 1892 on account of œdema and dyspnoea, and from that time until his sudden death in 1899 he continued its use in daily doses. During that time he travelled extensively, and was in fairly good health. Occasionally, after some unusual strain the dose had to be increased for a few days to obtain satisfactory diuresis, but the protective action of digitalis gave him a comfortable range of effort, and he suffered from none of the usual phenomena

¹ Archiv f. Heilkunde, 1876.

⁵ Charité Annalen, 1868, Vorlesungen über die Krankheiten des Herzens.

⁶ Les Maladies du Cœur.

⁷ Verhandlungen des Congresses f. innere Medicin, 1899.

⁸ Therapie der Gegenwart, 1899.

⁹ Ibid.

of heart disease. According to accurate records kept during the seven years, he took in that time 305 grams of digitalis.

As these are the only publications I can find on the use of digitalis in tonic doses, I feel justified in communicating my experience in this subject, collected from a large number of cases observed over a period of several years.

Looking over the records of these cases, I can distinguish two groups which have different prognoses and treatment. In the first group are the valvular lesions of rheumatic origin. It is principally in these cases that we derive the full benefit from the tonic action of digitalis. Then, the lesion once established, the heart has to overcome a certain constant resistance. An alteration in the compensatory mechanism is demanded only with an inter-current infection, rheumatic or otherwise.

In the second group are the myocardial and arteriosclerotic cases, in which the pathological processes are progressive. The heart has to increase its work constantly to compensate for the increasing loss of tonicity, to keep up excretion in the contracting kidney, and to overcome the high blood pressure.

Let me first consider the valvular lesions. In my series these are all at the mitral valve, and in most of them the stenosis is the preponderant factor. A typical example may be found in the following case:

CASE I.—Mr. M., aged forty-two years, came under my care on September 19, 1908. He had had two attacks of rheumatic fever fourteen and eight years previously, and five years ago he had an attack of gonorrheal rheumatism. Ever since that time he has been conscious of his heart, and gets out of breath easily. Nevertheless, he continued his usual mode of life, filling a very responsible and strenuous position by day, drinking and smoking very heavily at night. In December, 1907, he had an attack of influenza, which left him weak and not fully recovered. In the following June he noticed swelling of the legs and abdomen, and dyspnoea appeared. Jaundice had developed a few days before I saw him.

A diagnosis was made of mitral stenosis and insufficiency and tricuspid insufficiency. The pulse was permanently irregular—about 140 per minute; the blood pressure, difficult of estimation on account of the irregularity, was approximately 160 systolic, and 110 diastolic (von Recklinghausen, water pressure).

The patient received 0.7 gram of digitalis in the next four days. It was then discontinued, as the pulse had dropped to 60, with the onset of an enormous diuresis. At that time an early diastolic murmur could be heard; also a distinct reduplication of the pulmonic second sound. Though kept in bed all the time, œdema reappeared on October 9, with rales over the bases of the lungs. Digitalis was resumed, 0.1 gram being given daily. The result can be seen in the following table:

Date.	Digitalis.	Fluids. (24 Hours) Ounces.	Urine. Ounces.	Specific gravity.
October 2		24	30	1018
" 3		34	34	1020
" 4		36	40	1014
" 5		36	34 $\frac{1}{2}$	1014
" 6		36	44	1014
" 7		46	29	1016
" 8		36	35	1017
" 9	0.1	36	33	1016
" 10	0.1	42	32	1017
" 11	0.1	42	42	1015
" 12	0.1	36	49	1017
" 13	0.1	39	53	1012
" 14	0.1	36	62	1011
" 15	0.1	46	45	1012
" 16	0.1	39	36	1018

Note that the digitalis action appeared on the 11th, the third day of the treatment. The heart now seemed to be well compensated; the œdema had disappeared, and he was able to go about his business.

On October 29 some œdema reappeared, with enlargement of the liver. The dose of digitalis was immediately increased to 0.3 gram, with an increase in the diuresis and a dropping of the pulse rate to 68 next day; 0.2 gram was given that day, and the day after the usual daily dose was resumed. When seen on November 20, the heart was well compensated; there was a strong apex beat; pulse 68, no œdema. Blood pressure: systolic, 160; diastolic, .85. The pulse remained permanently irregular. On December 3 slight œdema of the legs appeared, and on the 6th the dose was again increased to 0.3 gram; 0.2 gram was given on the 7th, and on the 8th the regular dose was resumed. Diuresis and disappearance of the œdema followed on the 7th.

Since then the patient has remained well, attending to his business, and he has been fully compensated, except on two occasions, when some physical overstrain brought on swelling of the liver and slight œdema. On both occasions the disturbance yielded on the second day to the usual increase of digitalis. He has now been taking 0.1 gram of digitalis regularly every day for twenty months, and we see the typical result of such treatment. A heart which failed under the slightest provocation (October, 1908) has been toned up so that the patient has been able to attend to all of his duties without any symptoms of failing compensation.

Such experience has taught me to follow up the cumulative doses by tonic doses of digitalis in every case in which a rheumatic valvular lesion has led to heart failure. As soon as the full digitalis effect is obtained, usually on the second or third day, I give 0.1 gram and continue this as long as the patient is under my care. In this way I have kept a number of advanced cases fully compensated for many years.

As stated earlier in this article, tonic doses may be used to great advantage when slight œdema, and enlarged liver, and a decrease in the urinary excretion point to an imminent failure of compensation. I usually combine the treatment with rest in bed and restriction of food to 1000 c.c. of milk a day for a period of three to six days.

Let me now consider the value of this treatment in the second group of cases—the myocardial and arteriosclerotic. The prognosis in arteriosclerosis is not nearly so favorable as in valvular cases, especially if a complete breakdown has already taken place. The constant strain of the enormous peripheral resistance, and the direct interference with nutrition tend to a progressive diminution in the activity of the heart muscle. Thus, failure of compensation may appear with very little warning during the treatment, and there is none of the security felt in the valvular cases, where a break comes only after some unusual strain. When a break comes, the usual increase in dosage is demanded. On resuming the daily dose, however, we often find that 0.1 gram twice a day is needed. Soon even this will not postpone the day of reckoning, and larger doses are out of the question on account of cumulative phenomena.

This subject is well illustrated by the following history:

CASE II.—Mr. B., aged fifty years, a schoolteacher. During the last four to five years he has had occasional attacks of shortness of breath, which has become almost permanent in the last four months, and is aggravated at times by a dry, hacking cough. Considerable œdema has appeared in the last four weeks. Examination showed chronic nephritis, hypertrophy and dilatation of the left ventricle, mitral and tricuspid insufficiency, œdema of the legs, and swelling of the liver. Blood pressure was 240 systolic, 160 diastolic (von Recklinghausen); pulse, 121, regular.

Compensation was secured in six days with restriction of food to 800 c.c. of milk, and the use of 0.8 gram of digitalis leaves. The pulse fell to 80, and the blood pressure to 170 systolic and 85 diastolic. He was dismissed from treatment May 15, but returned on June 13, with œdema of the legs; pulse, 104; blood pressure, 221 systolic, 165 diastolic. He was given 10 drops of digalen three times a day until July 10, when it was discontinued, as there was no change in his condition. Full digitalis action was then obtained with the powdered leaves, 0.3 gram on the first day, 0.2 gram on the second and third, and 0.1 gram on the succeeding days. This time he remained well and fairly compensated for nearly a year. On October 14 his pulse was 84; blood pressure, 210 systolic, 125 diastolic, and there was no œdema. About this time he had two short attacks, with anginoid symptoms.

On May 15 of the next year he returned with considerable œdema of the legs; pulse, 120, slightly irregular; blood pressure, 210 systolic, 160 diastolic; heart considerably dilated, and the liver 5 cm. below

the costal margin. He was given 0.8 gram of digitalis in the next four days, with the usual result of diuresis and disappearance of the œdema. After this it was found necessary to give 0.2 gram daily. This preserved a balance for about four weeks, when the œdema returned, and death followed in a few days.

In the second group of cases there is one other symptom to be watched for with the œdema, the enlargement of the liver, and the rales, and that is gallop rhythm. Lately, Müller¹⁰ has again insisted on the importance of this as a sign of beginning failure, and an indication for the use of digitalis. I have followed this rule for several years with very satisfactory results. We practically never see this symptom with purely valvular lesions.

The following practical points should be observed in the use of digitalis in tonic doses:

Nothing is more important than that the digitalis should be physiologically active. Focke,¹¹ Gottlieb,¹² and Fraenkel¹³ have repeatedly urged the necessity for standardized preparations, and anyone who has seen the absolute inertia of the usual infusions, tinctures, and digitalins will heartily agree with them. Only three preparations are available for tonic administration. Groedel, in his first publication, advocated digalen, which is supposed to be digitoxin, and without any cumulative action. Fraenkel showed that digalen has the same cumulative action as any other preparation if given in corresponding doses. I have discarded digalen, because it has often failed to produce any effect when afterward another preparation succeeded—just as I observed in the second case reported herewith. Balfour has used Nativelle's digitoxin granules with excellent results, and I also have found them very reliable. The dose is 0.00025 gram every day, and the action becomes marked after ten to fourteen days.

For some time now I have prescribed almost exclusively Allen's English digitalis leaves in doses of 0.1 gram a day, and concur with Janeway¹⁴ in praising their uniform and reliable action. Secondary effects are rare, and I do not remember a single case in which the drug had to be stopped on account of stomach symptoms. In an experience of several years, I have seen but one instance of cumulative action with the daily dose of 0.1 gram. That occurred in Case I, herewith recorded, who developed the following symptoms after using the drug a year. There was a progressive slowing of the pulse from 80 to 68, and long silences of three to four seconds would be followed by a series of rapid contractions. The patient felt uneasy, was dizzy, and there was a considerable diminution in the

¹⁰ Münch. med. Woch., 1908.

¹¹ Berlin. klin. Woch., 1906; Archiv der Pharmacie, 1903.

¹² Zur Theorie der Digitaliswirkung, Med. Klinik, 1906.

¹³ Ergebnisse der innere Medicin, vol. i.

¹⁴ AMER. JOUR. MED. SCI., 1908, cxxxv, 781.

amount of urine. These symptoms disappeared upon stopping the digitalis. Such action can be avoided easily by giving the drug only three weeks out of four.

Probably the main reason why the tonic use of digitalis has not become popular is that men have feared that the body would accustom itself to the drug, so that the dose would have to be increased, and finally, there would be no action at all. Practical experience has shown that in purely valvular cases this does not occur; on the contrary, the dose may have to be reduced later, as described in the preceding paragraph. In the second group of cases, the dose had to be increased to 0.15 or 0.2 gram a day, but this was due to the progressive character of the process. Such an increase is shown graphically in the record of digitalis taken yearly by Kussmaul's patient.

Year.	Grams.
1892	15.00
1893	41.65
1894	35.10
1895	39.20
1896	44.48
1897	49.08
1898	57.86
To March 29, 1899	22.92

Experience has shown also that cumulative doses have exactly the same effect on patients who have been under tonic treatment as they have in similar cases in which digitalis is used for the first time.

We frequently have to consider the advisability of combining other drugs with digitalis. Many writers advise the giving of vasodilators to counteract the constrictor effect of digitalis. It is high time that we discard this hoary tradition and look squarely at the facts in the case. As mentioned at the beginning of this article, most of the work done on digitalis was with toxic doses, and vasoconstriction is one of the toxic effects. It has been shown clinically that in the majority of patients with beginning digitalis effect the blood pressure falls. Conclusive proof that digitalis in clinical doses relaxes the peripheral vessels has been given by O. Müller¹⁵ and his pupils, who showed with the plethysmograph that there is a constant increase in the volume of blood in an extremity after the use of digitalis.

The increase in blood pressure so frequently seen in failing compensation, even in mitral disease, seems to be due largely to the dyspnoea. The giving of digitalis leads to better ventilation of the lungs; more oxygen for the respiratory centre, and secondarily a fall in blood pressure.

Regular weekly to monthly determinations in all my cases have shown that the tonic use of digitalis has no tendency to increase the

¹⁵ Verhandlungen des Congresses f. innere Medicin, 1909.

blood pressure, but, on the contrary, a fall in the systolic pressure can often be noted coincident with an improvement in the general condition of the patient. Iodide has been used in conjunction with digitalis when it was deemed advisable. In anemic cases, when the general nutrition is badly affected, I have found the combination with arsenous acid very efficacious, and it may succeed when digitalis alone would fail.

CONCLUSIONS. 1. Digitalis acts as a specific on the tonicity of the heart muscle, and is indicated whenever symptoms point to a failure of that function.

2. Its tonic effects are best secured with a dose equal to the amount excreted—about 0.1 gram a day—though doses of 0.15 and 0.2 gram a day sometimes can be taken for weeks without the appearance of cumulative effects.

3. Loss of tonicity is shown first by general symptoms—rales over the bases of the lungs, enlargement of the liver, and slight œdema of the ankles.

4. Digitalis is indicated, therefore, whenever these symptoms appear, and especially in cases in which the patient, after recovering from a severe break in compensation, shows a tendency to fail on the slightest exertion.

THE TREATMENT OF TYPHOID FEVER.¹

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ETIOLOGY. Typhoid fever, which is one of the commonest diseases in our experience, but less common than in the experience of our medical fathers, thanks to the interest elicited by the work of the research scholar and an awakened sense of civic responsibility, is due to the invasion of the body by a definite bacterium, *Bacillus typhosus* of Eberth. The gross lesions are referable to the intestinal canal, but they are to be looked upon merely as local expressions of a general infection, just as lobar pneumonia is but a localization in the lung of an organism that infects the whole body. This is an important therapeutic concept, as it directs our attention to the individual as a whole and spares us useless effort to medicate the intestinal canal, in the hope of curing the disease. The mortality varies in different epidemics and varies in private and hospital practice, but on the whole is in the neighborhood of 15 per cent.

THERAPY. We are dealing with a self-limited disease, the cure of which depends on the elaboration of specific bodies by the tissue cells of the patient, a result we have not yet been able to duplicate

¹ A lecture delivered at the Cornell University Medical College.

in the laboratory. This does not mean that we cannot influence the course of the disease. On the contrary, a considerable fall in mortality has come about as the result of skilled care, conscientious watchfulness, competent nursing, and the application of definite measures to the relief of symptoms and complications.

REST. It would seem almost superfluous in a disease of such import as typhoid fever to insist on rest, but it must be remembered that the onset is slow, and in mild cases, or what at the beginning promises to be a mild case, the patient is prone to look upon it as an indisposition, and the physician may be uncertain of his diagnosis, and in the meantime the patient is on his feet, perhaps attempting to attend to his business, or at least protesting against the bed. These cases are the so-called "walking typhoids." Statistics have shown that these cases do not do as well as those receiving attention promptly, and it is probable that what might have been a mild typhoid attack has been converted, by lowering the resistance of the patient, into a severe or fatal case.

Where, then, suspicion is aroused as to the possibility of typhoid fever, the patient should not be permitted to waste his precious strength while one is awaiting the development of diagnostic symptoms or the result of blood examinations. He should be put to bed at once and prepared for what is likely to be a long siege. Real rest can be obtained only by careful and competent nursing, by the exclusion from the sickroom of all business cares and causes for anxiety, and refusal to make the sickroom a reception room for solicitous friends.

The patient is not to leave the bed to go to the toilet, or even to use a commode, but the bed-pan is to be insisted on. This trouble comes in the early days of the fever. It will be a source of argumentation and contention, but one's dictum must be firm, backed up by a few words of explanation. The need for rest, the need of sparing the tissues useless oxidation, is emphasized by the length of the disease.

BED. While remembering to conserve the strength of the patient, it must not be forgotten that the strength of the attendant ought to be economized, and in no way can this be done to better advantage than in selecting a bed on which the patient can be readily handled. The ideal bed is the half-bed, or single bed, of a convenient height, with strong woven wire springs and a firm springy mattress. A folded blanket will render the surface smooth. Over the blanket, is to be placed a sheet, a rubber sheet, and a draw sheet. Sheets should be drawn smooth, for freedom from wrinkles and dryness and cleanliness are great factors in preventing discomfort, and, in very sick patients, the formation of bedsores. Over the patient a sheet and a light blanket is sufficient; and one low pillow, not too soft, makes for comfort. The upper sheet should not be drawn too tightly over the feet of the patient, as is often done to improve the appearance of the bed, to the patient's great discomfort.

ROOM. The best room is the largest room, with the amount of light most gratifying to the patient; with sunshine in the colder months, and shade in the summer months. It should be well ventilated and free from encumbrances. A hardwood floor is best. If there are carpets, they should be protected in the vicinity of the bed, in consideration of contamination with secretions, which may occur in the ordinary handling of the patient. It is very desirable to have a bathroom near at hand, for the convenience of disinfecting and disposing of secretions, as well as for facilitating hydrotherapeutic measures.

If there is a balcony or piazza that may be approached from the room, it meets a great desideratum, for in summer the patient ought to be kept out of doors, and in winter I am convinced of the value of cold air in improving the nervous manifestations and general condition of the patients. I believe we shall use the open-air treatment for all infectious fevers with vast benefit.

The bed should be prepared by placing a blanket on the wire springs, and on this a rubber sheet, each extending well below and on either side of the bed. On these is placed the mattress, on which the bed is made as usual. Over the mattress and its coverings the blanket and rubber sheet are now folded like an envelope, thus preventing the entrance of air under the clothes. A hood is worn by the patient and a hot-water bottle placed at the feet; the nurses are dressed for out of doors.

When there is diarrhea and incontinence of the bowel or bladder, then more constant attention to the bed does not make the open-air treatment feasible. If the patient is very sick or is delirious, a nurse should be in the room day and night, as self-destruction has occurred in this condition.

CARE OF THE BODY. If a properly trained nurse is in attendance, she will exercise all those niceties of her profession with reference to the care of the patient's body and comfort, which will usually improve on one's own suggestions, but it is unjust to the patient to take that for granted, and a quiet survey of the situation and inquiry into the methods used is proper. However, all nurses are not properly trained, and all patients cannot afford the attendance of a nurse. Under these circumstances, one must know what should be done; one should write out explicitly what is to be done, and then see that the instructions are comprehended and successfully carried out.

The state of the patient's mouth requires constant attention, lest, from a foul condition, it become the source of infection of the mucous membranes and their lymphatic supply, the tonsils, the ears, and the lungs; and, upsetting the stomach, destroys the appetite. The teeth should be brushed two or three times a day. The mouth should be rinsed with water or boric acid solution (2 per cent. to 4 per cent.), or one of many mild alkaline and antiseptic washes, after each feeding.

If there is a heavy coat on the tongue, such may be removed by careful scraping with the edge of a whalebone. Especial care must be taken to get at the back of the tongue and remove thick mucus from the throat. The cotton swab on a toothpick is a ready means of getting at the dead spaces in the mouth, where food may collect and decompose.

If there is much sordes, and there are fissures, a mild antiseptic containing phenol is of value. Here is one recommended for the purpose:

R_y—Phenol solution, 1 to 20,

Glycerin āā 1 ounce

Boric acid, saturated solution 8 ounces—M.

S.—To be used as a mouth wash.

Bits of cracked ice are grateful, and the condition is much relieved if the patient gets enough water to drink. The nose is to be kept clear by the use of olive oil on a swab, to soften dried masses, and cleansing with boric acid solution or mild alkalines. Whether hydrotherapeutic measures are pursued or not, the body is to have a cleansing bath with warm water and soap and the sponge.

The formation of bedsores is the *bête noire* of a good nurse, and this she avoids by constant care of the skin. Moisture about the buttocks is quickly removed, the parts sponged with alcohol or alcohol and water, equal parts, and, if the buttocks have been much soiled, with a mild antiseptic solution—phenol, 1 to 40, for example. If pressure has been long continued, the skin is rubbed to improve the circulation in the part. The parts are then dusted abundantly with a drying powder, like any of the talcum powders used for toilet purposes. The skin of the whole back is treated in this way. Especial attention is paid to the sacrum, the anus, the buttocks, and the heels. The position of the patient should be frequently changed, not only to avoid bedsores, but to lessen the chance of hypostasis in the lungs.

If sores are threatening, rings are used to take the pressure off, but unless used intelligently, they may be more annoying than useful. If bedsores develop, it may be imperative to use a water-bed or air-bed. The excoriated skin may be covered with a drying powder, like aristol, or a bland ointment, like zinc oxide ointment. If more serious sores appear, they are to be treated on surgical principles.

At certain times and in certain places flies are a great annoyance to the patient, and, not only that, but a very real danger to other members of the family or vicinity, by their well-known ability to carry infection from the patient to the food or drink of those about him. Under such circumstances, screens in the room and over the patient are all-important.

This leads naturally to a consideration of the disposition of the secretions and disinfection of the patient's clothes and utensils.

DISINFECTION. The stools, the urine, the clothes, the utensils, the bath water, the sputum, and the vomitus have all to be taken into consideration. Stools may be disinfected by 1 to 20 phenol. At least twice the volume of the stool should be used, the stool well broken up and allowed to stand several hours. Chlorinated lime, too, is used. It must be fresh, as it soon deteriorates on exposure to the air. A 1 per cent. solution is required; or, to avoid making exact solutions, a handful is put in the pan with the stool and enough water to cover and mix it with. Bichloride is not reliable for disinfecting stools. Urine is disinfected with 1 to 20 phenol, using one-third to equal amounts. The lesser amount has been shown to be effectual after one and one-half hours' contact. 1 to 1000 bichloride, in volumes equal to $\frac{1}{15}$ to $\frac{1}{40}$ of the urine, standing for an hour and a half, is effectual.

Bath water may be disinfected by adding $\frac{1}{2}$ pound of chlorinated lime to a tub (200 liters) of water and allowing it to stand an hour.

Bed linen should be soaked in 1 to 20 phenol for two hours or in formalin, 3 ounces to a gallon, for twelve hours, and then thoroughly boiled. Bed-pans, urinals, rectal tubes, and rubber sheets can be disinfected in phenol 1 to 20 and allowed to soak in it.

Knives, forks, spoons, and crockery can be thoroughly boiled. Sputum is best burned; vomitus may be treated with phenol and lime.

Mattresses can be disinfected after the disease is over with dry heat, and the room should be disinfected.

The nurses should give tub-baths, wearing rubber gloves and a rubber apron. If given with the bare hands, and, indeed, after handling secretions, the hands should be carefully washed and soaked in 1 to 1000 bichloride.

It must be remembered that the administration of urotropin by the mouth disinfects the urine, but we should not intermit the precautions just named.

DIET. Everyone who has treated typhoid fever has felt that the most urgent problem he has to meet is the dietary. He has consulted authority with the result that he has come away more bewildered than instructed. He has been urged to maintain a low diet, lest too great a burden be thrust on digestive organs and tissues weakened by disease, or damage be done to the inflamed intestinal wall with the production of hemorrhage or perforation; on the other hand, he has been taught to give the patient great freedom in diet, lest strength be sacrificed as the result of starvation. He has read arguments for liquid food, for solid food, for stimulating food, for bland food, until in his despair he chooses some guide with whom he is more or less well acquainted, copies his directions with slavish exactness, and proceeds to feed all patients by this measure.

We are dealing here with a fever and a long fever, during which oxidative changes must be met, either at the expense of food ingested or of the body itself, and during which extensive tissue destruction

is going on as the result of the disease; this must be made good by the food or the deficit will increase continuously up to convalescence, or bring about a bankruptcy, before convalescence can be attained.

The first great fact to be kept in mind in all fevers is that the body demands as much energy and heat in terms of heat units in fever as it does in ordinary rest in health; we will say 33 calories per kilo, or some 2300 calories for a man of 70 kilos, or 154 pounds; and that as a result of the fever itself, he usually needs some 25 per cent. more, or about 40 calories per kilo, or some 2800 calories for a 154-pound man. Therefore, he ought to get 2800 calories to meet this need from his food, unless he takes it out of his own body.

The second great fact with reference to the body needs to be met by the food, is that there must be a certain minimum of protein in the diet. Voit's standard was something over 100 grams per day, but more recent work has shown that even less would do, but that some 70 grams should be afforded. This demands intelligent scrutiny of the food, with the knowledge of its composition, in order that this minimum should be observed; or, what is next in importance, that it should not be too much overstepped.

The third great body of facts, in dealing with diet in fever, are those which inform us of the loss of protein to the body in fever and how to shelter it by the food administered. The wasting after fever, even a short fever, and so emphasized after a long one, is one of the most familiar phenomena of disease. The wastage is, of course, due to loss of both fat and protein, but more especially, from the standpoint of importance, of protein.

The destruction in fever may be assigned to three particular causes: (1) Starvation. There can be no doubt that our patients are, in too many instances, underfed. That this cause for protein loss can in a goodly measure be prevented goes without saying. (2) Fever itself. Pyrexia exerts a destructive action on protein of the tissues, as can be determined by studying the nitrogenous output in fever induced artificially, as in hot baths or by puncture of the floor of the fourth ventricle. In disease, however, it is not always easy to separate it from: (3) toxic destruction, meaning the breakdown induced by the toxins of the infecting organisms, in part autolytic, perchance, but the detail of which is still obscure.

The influences of pyrexia can, to a certain degree, of course, be influenced by hydrotherapeutic and other antipyretic measures. The effect of the toxins, until we have specific sera or other specific measures at our command, however, are not under our control; and yet, it is the purpose of this thesis to show how near to a nitrogenous equilibrium a patient can be brought, in the face of this toxemia, if supplied with the proper food in the proper manner.

I am indebted to Dr. Shaffer and Dr. Coleman¹ for many state-

¹ Archives of Internal Medicine, vol. iv; Jour. Amer. Med. Assoc., 1908, li.

ments of facts made here, but they are not to be made responsible for any conclusions I may draw.

In the disease in question wasting is marked. A loss of 10 pounds is slight, but losses of 40, 50, 60 pounds or more may occur. In this loss, nitrogenous tissue takes a large share. Cases in which the nitrogen loss has been studied, show the equivalent of 7 pounds of pure muscle tissue in twelve days, of $5\frac{1}{2}$ pounds of muscle tissue in eight days, and not rarely $1\frac{1}{2}$ pounds of muscle tissue in a day. This loss may mean not only a deprivation to the body of the functions this tissue subserve, but also disturbances, perhaps toxic in character, induced by the effort to katabolize this protein. The nitrogen partition offers similarities to those seen in the toxemias of pregnancy, and, to quote Dr. Shaffer's words, "there are severe so-called toxic cases of typhoid fever which terminate with acute yellow atrophy of the liver, a condition which appears to be closely associated with a particular type of faulty protein metabolism."

This loss can be avoided, to a greater or less degree, by the food. In considering the foodstuffs, fat, carbohydrates, and protein, one would naturally turn to the proteins to make good a loss of proteins, and, indeed, that is necessary, but to no such degree as would be anticipated. There must be enough protein to meet the daily needs under ordinary circumstances—the 70 grams of which I spoke. There may be a slight storage of excess, which does not obtain in health, but if we give a frank excess, it must be destroyed and eliminated by the organism, and more than that in the process of its katabolism, by virtue of what is known technically as the "specific dynamic action," gives rise to a large amount of heat, which cannot be utilized for the purposes of the body, and extra burden is placed to dissipate the heat. The result is that about 140 calories of protein are required to secure 100 calories available for the purposes of the body.

Fat, on account of its well-known tendency to induce digestive disturbances and diarrhoea, must be used sparingly. According to the best known investigators in this field, the strongest sparsers of body protein are the carbohydrates, and it is upon these that we place our reliance to solve the problem. It has been shown that the absorption of the fats, carbohydrates, and protein in typhoid fever, when severe diarrhoea is not present, is within 10 to 15 per cent. of normal, and Folin has shown that the absorption of the carbohydrates in this disease is practically normal.

In the feeding experiments carried out along this line of reasoning, among the typhoid fever cases in the wards of Bellevue Hospital the carbohydrate selected was milk sugar, because it ferments with difficulty and is less sweet to the taste than cane sugar and more soluble than the starches. The experiments showed that a nitrogen gain could be attained when the protein intake amounted to 75 to 85 grams, while at the same time the caloric content of the food was

high, 3700 to 3900, or 70 to 73 calories per kilo; that is, enough protein was used to meet the daily needs and the loss of nitrogen was stayed by the high carbohydrate content of the food. When the same amount of protein was used with 32 calories per kilo, the loss was considerable. When only 16 grams of protein were used, but with 62 calories per kilo, the loss was greatest.

Now, in one of our most recent and authoritative systems of medicine, the diet advised is 4 to 6 ounces of milk every four hours, or 24 to 36 ounces a day; the whites of one or two eggs every four hours, making the whites of six to twelve eggs a day. Taking the larger amounts, and granting that the patients were fed night and day, we should have 730 calories from the milk, and, allowing 60 grams as the weight of an average egg, two-thirds of which is white, we should have in twelve eggs 480 grams. Of the white, 12.5 per cent., or one-eighth, is protein; the fat and carbohydrate almost negligible. That would give 60 grams of protein from the eggs, or 246 calories. These patients would get at the most 1450 calories, or about one-half their theoretical requirement. Of protein, they would get about 100 grams, a sufficiency, if backed by enough carbohydrate. This diet has been shown, in the Bellevue patients, to be accompanied by a large negative nitrogen balance. There may be theoretical considerations for such a low diet in typhoid fever, but I do not think that they have any scientific basis.

The more liberal feeding which has always been insisted on by individual clinicians, who, however, formed a small minority, is in the hospitals of New York today finding more advocates. The dietary at St. Luke's Hospital, contains on an average 63 ounces of milk to which 1 ounce of milk sugar is added, and three whole eggs a day. This diet contains 2585 calories, about 1000 less than Shaffer's and Coleman's and about 85 grams of protein.

The basis of the high caloric diet as used in the wards of Bellevue Hospital is milk, cream, eggs, milk sugar, bread, and butter. A quart of milk affords 650 calories. A quart of cream (20 per cent.) about 2000 calories; each egg 60 to 70 calories; milk sugar about 120 calories to the ounce; white bread, home-made, about 1225 to the pound—that is 100 calories to a thick slice of $1\frac{1}{4}$ ounces; butter about 3600 calories to the pound, or 100 calories in a pat a trifle under $\frac{1}{2}$ ounce. With such materials various combinations may be made: $1\frac{1}{2}$ quarts of milk will give 1000 calories, a pint of cream 1000, $\frac{1}{2}$ pound of sugar about 1000 more, four eggs 250 more, thus making 3250 calories. If one wants a few calories more, 250 to 500 more can be gotten in 2 to 5 ounces of sugar added to lemonade..

A glass of milk that contains 7 ounces of milk, 1 ounce of cream, and 1 ounce of milk sugar, offers about 325 calories. Eight such glasses in twenty-four hours will give 2600 calories, as high as many care to go. The protein, as well as the calories, in this food must be remembered. The milk contains 35 grams to the quart, and

the cream a trifle less, 25 grams; the eggs, 8 or 9 grams; the bread, about 9 per cent., or 45 grams to the pound loaf. In the more liberal dietary just suggested, about 100 grams are afforded; in the smaller, 70. Two eggs added to this would increase the protein to 85 grams.

Dr. Shattuck, of the Massachusetts General Hospital, has long advocated a more liberal dietary in typhoid fever, and can point to quite as good results as the advocates of a restricted or milk diet. I will not cite his dietary in full, but will mention some of its items, which show one how varied we can make our patient's food and relieve a monotony that threatens a loss of appetite and gastrointestinal disturbances. These are milk and the various milk products, some of which are better borne than others, such as buttermilk, koumys, matzoon, whey or milk with tea, coffee, or cocoa; or the milk can be diluted with lime water, Apollinaris, or Vichy; soups of beef, veal, chicken, tomato, potato, pea, bean, or squash, strained and thickened with powdered rice, arrowroot, flour, barley, or egg; gruels, ice-cream; eggs, soft boiled or raw, or eggnog; finely minced lean meat or scraped beef, soft crackers with milk or soups, soft puddings, soft toast without crusts, blanc mange, wine jelly, apple sauce, and macaroni.

Many of these articles have a low calorie content, and would not serve the purposes of our new teaching, but they show what is safe and what may be used to diversify the dietary.

Each patient must be carefully studied with reference to his dietary. We can make a mathematical problem of his food needs, but not of him. If he is highly toxic and stuporous, if he has gastrointestinal disturbances, we cannot expect him to ingest or digest the same quantity and quality of food that he would if his disease was of a milder type. We wish to avoid the older policy of frankly starving our patients, while we at the same time do not desire to stuff them like a Christmas goose, willy-nilly. I believe if the patient is moderately or severely ill when he comes under our observation, we should begin on milk for the first twenty-four hours, some two quarts; then a little milk sugar, a dram to a glass, and rapidly more as he shows that he handles it well; and at the same time or shortly after, a little cream—a half ounce to an ounce to a glass, watching this with especial care; eggs, gruels, or soups, bread or toast or crackers, ice cream, cup-custard, or other milk modifications. If the milk is not well borne, milk preparations, such as koumys, matzoon, buttermilk, or whey, may be used.

If the tongue is coated, if there are eructations, or if diarrhœa sets in, the cream should be stopped and the milk skimmed. Of the meat soups, one may say that they have little caloric value, but may improve the appetite. The scraped or minced meats may be allowed, if greatly desired, but they are not an economical form of food in fever, owing to their high specific dynamic action, and should

not be given in the severe toxic cases, as it is believed, on fair grounds for such an assumption, that the liver in some of the cases is impaired and unable to metabolize the protein of the food brought to it in the normal manner.

At any rate, in such cases the urea nitrogen decreases while the "rest nitrogen" increases, and the giving of meat aggravates the condition and furnishes us in the convalescence of severe cases the so-called "febris carnis," as Ewing and Wolff believe.

I believe a patient should be given as much food as he will take and handle well. If he will take 4000 calories, he should have it; but with the earliest signs of gastrointestinal disturbance or disgust for food, one should diminish the food, and do so promptly. The patient's appetite is a valuable guide, and within the range of food mentioned, his likes and dislikes should be considered.

HYDROTHERAPY. If one had a brief to hold for hydrotherapy, he could not do better than to appeal to its application in typhoid fever. So thoroughly convinced is the American practitioner of its great value in this condition that arguments to maintain this thesis are only of historical value. The mortality of typhoid fever, vary as it may in different epidemics, hospitals, and localities, has, under the old expectant treatment, amounted to 15 per cent. the world over. Since the introduction of the cold water treatment, where large numbers of cases can be collected, as in great hospital services, the mortality has been cut in half, running about 7.5 per cent. with wonderful uniformity in the hospitals of our larger cities. Statistics have no value unless applied to large numbers. For example, in a certain hospital some 100 cases of typhoid were treated by the bath, with a mortality of 1 per cent. One might have attributed this success to some perfection of technique not prevailing elsewhere, but when the same clinician had collected 400 cases his published mortality showed 7.8 per cent., or that of the general experience.

The hydrotherapy of typhoid fever, as universally adopted in this country, is based on the Brand bath, or a modification of it, and the greater the modification, the less successful it seems to be. Two emphatic statements with reference to this bath should be made: (1) The essence of the bath lies in the application of cold water and friction, neither one nor the other alone, but both; (2) the purpose of the bath is to improve the condition of the poisoned centres and organs: the heart, lungs, kidneys, and centres in the brain and medulla; incidentally, and to a degree beneficially, to reduce temperature. The last is too often put first, which in this instance does not have biblical justification.

METHOD. The body should be immersed to the neck; the bath should be given preferably in a tub. In hospital practice, a portable tub on wheels is used. In private practice this is, as a rule, too cumbersome, and a tin bath tub may be used, elevated to nearly the

level of the bed on wooden horses, blocks, or other contrivance. Placed alongside of the bed, the floor being protected by a rubber sheet, oilcloth, or carpet, it is filled three-quarters full of water, with buckets, or a hose attached to a tap, if one be conveniently near.

The patient's nightshirt is removed, his genitals covered with a napkin, bound about the body, or the whole body covered by a sheet, under which he is bathed, which latter method is a little more awkward. He is given a half ounce of whisky, or a cup of hot strong coffee (4 ounces), the face bathed with cold water, a folded bandage a couple of inches wide, bound around the forehead and tied below the occiput, to keep the water applied to the head from running into the eyes and streaming down the face, and he is then ready to be lifted into the bath. To do this, the best way is for one attendant to rest the patient's head on one arm while he raises the upper part of the body by lifting under the shoulders, while another attendant lifts the lower extremities, the patient being requested to stiffen himself out.

Another method, which has advantages if the patient is very stuporous, is to spread a hammock netting under him or a strip of canvas with straps attached, and lift him on this into the tub and by the same means out of it. The head should rest on a water-cushion ring or air-ring.

As soon as the patient is immersed in the bath, the equally important part of the procedure is begun—the friction, gently applied (not kneading) to all parts of the body except the abdomen. The back must not be forgotten. At intervals during the bath, cold water, at 50° F., should be poured over the head. While in the bath the bed should be prepared for his reception, by placing on it a double blanket, on the side he will occupy; a pillow is covered with a towel, the blanket is covered with a linen sheet, and hot-water bottles are placed at the foot.

The patient is then lifted onto the bed, the napkin is removed, and he is surrounded by the sheet, the edges and ends being tucked about the neck and under the arms. He may be allowed to lie in the sheet for five or ten minutes and then dried with soft towels, or more immediately if the temperature is low and he is shivering. The tub is best emptied by a siphon.

The temperature of the water Brand set at not more than 70° F., and not less than 65° F. The frequency he advised was every three hours, if the rectal temperature was above 102.5° F.; the length of the bath, fifteen minutes. These rules laid down by Brand have met with but slight modifications where satisfactory results are obtained. Slightly lesser temperature of water is used at times, a little higher temperature of the body taken as the indication of the bath, and the initial bath begun at a milder temperature. At St. Luke's Hospital, in New York, the tub bath is given at 80° F., and in selected cases as low as 70° F. The bath is con-

tinued fifteen minutes. It is given every four hours, if the rectal temperature is 103° F. At the Presbyterian Hospital, in New York, the tub bath is given at 85° F. for ten to fifteen minutes, at four-hour intervals, if the body temperature is 102.5° F.

It is fully appreciated by the advocates of the Brand system that the reaction to a bath at 65° F. cannot be anticipated in markedly toxemic cases, so that a patient seen in the third week or latter part of the second, who is very toxic, should be subjected to a bath of higher temperature (75° F. or 80° F), and for a shorter time. Our hospitals rarely get patients in the first week, and the higher temperatures adopted are better suited to their class of cases.

If a tub bath cannot be obtained, a substitute for one can be constructed in the bed by running a clothesline around the bed, at a suitable height above its level, attaching a rubber sheet to it by clothes-pins, thus making a tub of the sheet. Other contrivances can be resorted to, to approximate a tub in the bed, as building around the sides and foot and head with rolled blankets, and the use of the rubber sheet as the receptacle for the water. When the patient is put in the water one expects a sudden shock, deep breath, and gasping. These are in themselves beneficial. The patient may shiver, the skin may be shrivelled, and the nails cyanotic, and yet not contraindicate the bath; but if the face is cyanotic, shivering marked, and chattering of the teeth occur, and the patient does not react well on being taken from the bath, then the next bath should be at a higher temperature and less long. Cyanosis of the face or threatened collapse should lead to immediate removal of the patient, warmth to the body externally and internally, and stimulants—hot coffee or hot whisky.

Many untoward symptoms in the bath are due to failure to appreciate the value of, and failure to apply properly the friction during the bath.

The benefit derived from the bath is very obvious and is expressed by improvement in the functions of various organs. No benefit can be expected from any procedure applied to the moribund, and the greatest success in the treatment of typhoid fever by this method is in the early application of it. Many of the severe symptoms seen in cases coming under observation or treatment late, are not observed at all in the cases bathed the first week. The most characteristic effect clinically of typhoid fever is the toxemia impinging on the brain, inducing restlessness, sleeplessness, delirium, stupor, and subsultus tendinum. The stimulating effect on these centres, receiving sensations pouring in from every point of the periphery and nourished by a better blood supply, is shown by an amelioration of every one of these symptoms, better sleep and more quiet, and a clearer mind more alive to its environments.

In typhoid fever the pulse is slow; when rapid, ominous; it is often dichrotic, bespeaking a low vasomotor tone. We stand in

dread of heart failure, but the opinion prevails today that in acute infectious diseases the heart rarely fails, but that the vasomotor apparatus is the first to falter.

After the tub, the pulse is smaller and harder, losing its dichrotism; the pressure increases by 15 to 20 mm. Hg., and the rate falls. All this is very real, and may be attributed, in all probability, to the effect exerted on the vasomotor centres, though the tonic effect on the vascular walls of the periphery is undoubtedly a factor.

On the respiratory apparatus a beneficial effect is exerted by the fact that the contact with the cold water causes the patient to take deep breaths, which lessen the danger of passive congestion and hypostatic pneumonia that threaten in severe cases. More than that, the respiration of the tissues is enhanced, as increased oxidation can be demonstrated by measuring the oxygen intake and the CO₂ output.

The contact of the cold water and the friction improve the circulation in the skin and so improve its functions. The improved condition of the circulation increases the elimination of urine and the toxins of the disease. The temperature is lowered, but this is no longer considered the object of the treatment, and often in the height of the disease the temperature is not influenced, but striking improvement in the general condition is attained, in terms just given.

After all, it is the individual that is being treated, and this means that a precise procedure cannot be the optimum for every case. Higher temperature of the water and shorter baths are required for those who stand the shock of the typical bath poorly, for those toxic and advanced in the course of the disease, and for children.

Contraindications for the baths comprise hemorrhages and signs attributable to perforation or peritonitis, all of which conditions demand absolute rest until the proper procedure, surgical or otherwise, can be carried out. Cholecystitis, phlebitis, pleurisy, if accompanied by considerable pain, contraindicate the bath for a like reason. Cyanosis and syncope demand cessation of the bath in which they occur, but if the case is a severe one, the use of water may be continued in a milder form of application. Large bedsores, because of the difficulty of properly treating them, contraindicate the bath. Bronchitis, pneumonia, the milder grades of kidney involvement, and menstruation and pregnancy do not call for a change of procedure.

Beside the full bath of Brand, there are certain other methods of applying water in this disease. A slight modification of the Brand bath is the so-called graduated bath of Ziemssen. The details are the same as for the Brand bath, except that the water is warmed to 90° F., and then, after the patient is in the bath, is cooled down to 70° F. by adding cold water as the bath proceeds. The bath lasts half an hour with friction. This is a suitable procedure for those who stand the bath poorly, or think they do, and refuse the colder bath, or the very toxic cases of the later stages, or children.

When, for any reason, it is not feasible to use the tub, an approximation to the methods and results of a tub are attained by what is sometimes called a slush. The patient is stripped, a rubber sheet of ample proportions is put under him, the edges of which are elevated by pillows and blankets folded to the formation of a trough. Water is poured into this trough and the patient given a bath with friction, as in a tub, while cold compresses are kept at his head. The water, of course, becomes warm rapidly and is kept cold by adding bits of ice. The temperature cannot be so accurately regulated as in the tub. The head of the bed is elevated, the water drained off, the patient rubbed with a little alcohol, or alcohol and water, after drying and removing the rubber sheet, and then dusted with talcum. These slushes may be very effectual when properly given.

When the baths are refused, or for other reasons cannot be given, packs and sponges may be substituted; but, while these afford comfort and do some good, they fail in the general stimulating effect that comes from the friction of the body immersed in cold water.

CARE OF THE ALIMENTARY TRACT. In the routine treatment of typhoid fever there are no organs whose functions have to be so jealously guarded as those of the alimentary tract, not only because failure of digestion and absorption threaten a fatal issue in so long a disease, but because insufficient elimination and excretion heighten the toxemia, and because diarrhoea exhausts and hemorrhage and perforation await upon the advance of the local lesions. Constipation is almost constant in typhoid fever as we see it in New York. Diarrhoea, which one might gather from any of the text-books as characteristic, is rather the exception.

If seen early, a catharsis of castor oil, 1 ounce, or Epsom salt, 1 ounce, may be given. If seen late, all catharsis should be avoided. Enemas of tepid water, of soapsuds, or, in obstinate cases, soapsuds with an ounce of sweet oil, or castor oil, should be given every other day. It is the lower bowel one wishes to empty, not the upper, and this can be done effectually with the enema. The upper bowel, the site of the lesion, like any other inflamed part, should be given as much rest as is compatible with its physiological functioning.

The lower bowel is physiologically differentiated; the lower part forming the reservoir for undigested food, and, what is more important, the excreted matter, the nitrogenous content of which forms an almost constant portion of the total nitrogen output; it is, too, the site of active bacterial action, and is an absorbing surface. We wish to avoid absorption of toxic material of bacterial action, which may add its burden to the already overloaded blood. Nothing is more surprising than the large stools obtained from patients on a milk diet, and still more, the considerable movements obtained when patients are taking little or no food. The patient's plea to

avoid the enema that he has taken nothing, therefore, can have nothing to evacuate, must be met by explanation of the physiological fact and demonstration of its accuracy.

Tympanites, to some degree, is almost constant, but when marked is usually the expression of the severity of the intoxication. This parietic condition of the bowel, which allows the collection of large quantities of gas, is rife with danger, as it increases the chances of hemorrhage and perforation, and interferes with respiration and cardiac action; pain may be an accompaniment. The free use of water, the attention to periodical evacuation of the bowel, and the general tonic effect of the baths, lessen the severity of this complication. When, in spite of such precautions, it does obtain, the following measures may be carried out:

1. Introduce for a distance of 12 to 15 inches into the bowel a soft, pliable rubber catheter, taking great care not to use force. The larger bowel is, as a rule, more implicated than the smaller. This will at times permit the escape of considerable amounts of gas. It should be left in ten to twenty minutes, or even a half hour, and may be repeated every two to four hours, as indicated. Turning the patient while the tube is in place may facilitate the escape of gas.

2. The use of stupes. Two or three thicknesses of flannel are wrung out of hot water, as dry as possible, and applied every three or four hours. The technique is as follows: A flannel roller is put under the patient, the abdominal wall smeared with vaseline, the stupes applied, the edges being turned under to prevent dripping; oil silk applied, and the roller brought up over the stupes in the manner of a binder. This should be changed every two or three minutes for ten or fifteen minutes, or every ten or fifteen minutes, for several hours.

3. Turpentine. There are three ways of administering turpentine to relieve this condition: First, in the stupes, by adding a dram of turpentine to the hot water into which the flannels are to be dipped; by sprinkling the stupes with turpentine; or by very lightly passing a bit of absorbent cotton wet with turpentine over the abdomen before applying the stupes. Care must be constantly exercised not to irritate or burn the skin. Careless application of the turpentine will certainly entail such trouble. The second method is by giving turpentine enemas. One-half ounce to an ounce of turpentine is to be used in one pint of soapsuds enema. The method is as follows: Take a little hot water and a piece of Castile soap; make a thick soapsuds; add the turpentine slowly, constantly stirring. This makes an emulsion. Add the pint of water, and the emulsion remains stable. Oil enemas are made in the same way. The third method is by the mouth; 10 to 20 drops are used every four hours. It is sometimes dropped on loaf sugar, but the turpentine makes the sugar tough and not easily soluble. It is better given in capsules, 10 minims each, or in emulsion, to

which a little oil of cinnamon may be added as a flavor, while at the same time it adds to the effect of the turpentine. Thus:

R \bar{y} —Olei terebinthinæ rectificati	10
Olei cinnamomi	q. s. (or 3)
Acaciæ	q. s.
Aq. destillatæ	q. s.
M. et fiat emulsum	60
Sig.—One or two teaspoonfuls.	

Sometimes a large flat ice-bag or the ice-coil, brings relief, and if all these measures fail, a hypodermic injection of eserine salicylate or sulphate ($\frac{1}{50}$ grain) may be tried. The diet should be materially decreased, milk stopped, and albumin water administered, and water given freely, if the condition is severe.

Diarrhœa, fortunately, is not a common complication in typhoid as we see it here. Two or three loose movements a day do not call for interference, except in the matter of regulation of food. The food and neglect of the bowel may be the inciting causes. If the patient is on a milk diet, the fat is more likely to be responsible for the diarrhœa than any other constituent of the food, and should be removed. Scalding the milk may help. If the diarrhœa is severe, the food should be cut down. Of the astringents, bismuth is the best, and should be given in sufficient doses (30 grains) every two or three hours. This must not be kept up too long, or if administered over a long period, it must be remembered that the bismuth may be retained in the bowel in such quantities as to produce irritation by sheer weight, while the diarrhœa still continues; hence, the necessity for irrigations.

Prolonged saline irrigations, by improving diuresis, lessening toxemia, and keeping the bowel clear, may be of distinct advantage. It is tempting to use opium, but it cannot be too emphatically insisted upon that by so doing, pain, the earliest and most important symptom of perforation, may be lacking—to the patient's undoing. It should not be used unless exhaustion from diarrhœa and increasing danger of hemorrhage and perforation from peristaltic unrest seem to demand it. Then one may give a few large doses, rather than long-continued small ones; for example, a pill of opium ($\frac{1}{2}$ grain) every two hours for three or four doses, or some such marked astringent mixture as one of our well-known clinicians has advised:

R \bar{y} —Pulv. opii	0.25	(gr. $\text{iii}\frac{3}{4}$)
Pulv. camphoræ	1.00	(gr. xv)
Plumbi acetatis	3.00	(gr. xlv)
Bismuth. subnitrat.	30.00	(oz. j)
M. et div. in chart. no. xv.		
Sig.—One every four hours.		

Gastric distress and vomiting are not common. If vomiting does occur, the milk should be skimmed; or, if severe, stopped. Cracked ice, in small pieces, sucked, may be of avail. Then try a mild

mustard paste to the epigastrium, one part in four of flour. If these do not succeed, try a bland powder of cerium oxalate (3 grains), sodium bicarbonate (5 grains), and bismuth subnitrate (10 grains), every two hours. If very severe, cocaine hydrochloride ($\frac{1}{5}$ grain) in tablet form, or one teaspoonful of 0.1 per cent. solution every two or three hours. Finally, stomach washing may succeed when other measures have failed.

Few things are more trying than meeting the danger arising from hemorrhage and perforation. Few occurrences demand more judgment and common sense than treating the hemorrhage of typhoid. To judge by the advice given by some authors, the appearance of hemorrhage is to be treated like an invading foe, to be met with every weapon at our command, from stiletto to bludgeon; while more timid counsellors urge letting it severely alone, lest by interference we come off worse than before. In the first place, in the early stages, a little blood may appear in the stools, resulting from an oozing of the hyperemic patches, and such small amounts at such a period need no treatment. In the latter part of the second week, and during the third, we are anticipating the hemorrhages of real significance from the ulcers and know that they do occur in about 7 per cent. of the cases. If the hemorrhage is mild, that is, small in amount, or well borne by the patient, we may have no premonition of it until the stool shows the red blood of the recent bleeding, or the tarry stool of one occurring some hours before.

In these cases, the present bleeding is of less importance than that which may occur later, so that our treatment is largely prophylactic. We cut down the food, we enjoin absolute muscular rest on the part of the patient, and turn him gently when required.

We may apply a light flat ice-bag or coil to the abdomen. We may give calcium lactate in doses of 10 grains three times a day, and in the light of our recent knowledge of the effect of horse serum on coagulation, we may give a dose of 10 to 20 c.c. of it; or, failing that, diphtheria antitoxin in similar amounts. To get the best results from the serum, it should be as fresh as possible. The old serum loses much of its potency in this respect. If fresh horse serum is not available, fresh rabbit's serum may be used.

Antitoxin, because it is likely to be old, is less valuable, and when a concentrated antitoxin made from the globulins, of no use at all. The same precaution must be used in administering the serum for this purpose as when giving antidiphtheritic or antitetanus serum, to avoid the results of anaphylaxis. To prevent this, a dose of 10 minims is given, which will be enough to produce sufficient evidences of anaphylaxis if it exists, but not a fatal result. If no manifestation appear in a half hour, the full dose may be given with more assurance. An initial dose of serum after a matter of ten days is likely to establish an anaphylaxis, and this precaution is doubly necessary, when a second dose is given after such an interval. Immunity

against anaphylaxis may be established by giving doses of serum—full doses—every day, or second day.

If the 10 minims cause anaphylactic manifestations, wait a couple of hours and give another 10 minims, and a third and a fourth at the same intervals. If no further symptoms appear, the large dose may be given.

If, however, the hemorrhage is severe, as shown by the large quantity of blood passed by the bowel, and even more if general symptoms of hemorrhage prevail, with or without the passage of blood—that is, sudden fall of temperature, pallor, cold sweat, cold extremities, rapid thready pulse, restlessness, and air-hunger, more decided measures must be taken. There is one drug that is of greater value than any other, namely, morphine.

It is to be given in doses of $\frac{1}{2}$ grain under the skin. Morphine is not a styptic, nor has it any effect on the caliber of the vessels or coagulation time, but what it does do is to afford the maximum amount of rest, both to the bleeding bowel and to the anxious brain, and to the restless and uneasy body, whose useless movements keep up the blood pressure. This gives the bleeding vessel a chance to do what it is trying to do—form a clot. It is pointed out that perforation occurs in these hemorrhages—one-fifth of the perforations; and that the use of opium blinds the symptoms, and no doubt it does, but, while anticipating such a complication, we cannot sit by and see our patient die from the hemorrhage.

There are many cases that come between these two extremes, and success in these cases is the fruit of experience and judgment. One can only say, when a patient is to be under constant observation for some hours to come, as he ought, hold off the opium as long as possible. If circumstances will not permit remaining by the patient, one should not spare the opium.

The bowels should not be moved for some three days after a hemorrhage, and then with caution. One should get back on the diet slowly and combat meteorism.

When the hemorrhage causes exsanguination, it must be treated like any other hemorrhage—elevation of the foot of the bed, heat to the extremities, saline infusions of 0.9 per cent. sodium chloride solutions, or transfusions.

Even more dangerous than hemorrhage is perforation. It occurs in 2 to 3 per cent. of the cases and causes some 12 per cent. of deaths in typhoid fever. It seems to occur as frequently in cases treated with the bath, but because of the lower mortality of the disease so treated, the percentage of death from perforation rises. If one in eight or more of the deaths in typhoid fever are due to perforation, it becomes a moral obligation to know the signs well. One will recall the sudden onset, with acute abdominal pain, like a bolt out of the blue; its paroxysmal character, the rapid rise in the leukocytosis, the two most important early symptoms, I think; then the

change in respiration, rapid pulse, distressed expression, local muscle spasm, rigidity, tympanites, with, perhaps, obliteration of the liver dulness.

Every attack of abdominal pain should mean perforation until continuous observation convinces otherwise, for thus its occurrence will not be overlooked. When it occurs, the surgeon should be summoned, an operation performed, and the perforation closed. If satisfied that pain has no such significance, then the ice-bag or stupes, or a light application of the cautery or small doses of bromides or codeine may be used; or, if more severe, small doses of morphine.

The cerebral disturbances are characteristic of this disease. In the early stages there may be much headache. This is best treated by the ice-cap. Sleeplessness is another common occurrence, and, as has been explained in considering rest, a symptom to be combated. Hydrotherapy properly applied mitigates this to a great degree. Small doses of bromides may be used, or trional in 15 to 20 grain doses, or chloralamid in 20 to 30 grain doses; but if it is marked and prolonged, morphine is the best drug to use. Delirium and stupor are best met by the baths. In all decided cerebral symptoms, help may be obtained from the tepid bath, with cold water poured over the head; from the ice-bag, from morphine, and, finally, when the delirium is great or the stupor deep, from lumbar puncture, an easy and innocent procedure. Draw off 20 c.c. at least, and more will do no harm, though headache may be aggravated by draining the cord. No delirious patient should be left alone for a moment. Restraint by sheets or other devices are sometimes needed.

CIRCULATION. When the characteristically slow pulse of typhoid fever becomes rapid, going above 100 to 110 to 120, our concern is elicited. If the heart is weakening, we shall get a poorer quality of first sound, perhaps evidences of dilatation and mitral insufficiency, poorer quality of pulse, and a fall in blood pressure. A sufficiency of diet and the hydrotherapy do much to prevent this disaster. If, however, the condition supervenes, stimulants must be given: digitalis in the form of infusion (2 drams four times a day), watching carefully for evidences of its physiological action, which, when obtained, indicate its cessation for a period, as the drug is slowly eliminated. If it cannot be taken by the mouth, on account of gastric disturbance, or when the demand is more urgent, diaglen may be used hypodermically in doses of 10 minims every four hours, or strophanthin ($\frac{1}{60}$ grain) intravenously or intramuscularly; strychnine, too, may be tried, in doses of $\frac{1}{30}$ or $\frac{1}{40}$ grain, every four hours, by the mouth or under the skin, according to circumstances. Caffeine, sodium salicylate (3 grains) every four hours, given in the same way, is even more reliable.

In threatened circulatory collapse, the more rapidly acting stimulants, as camphor (3 to 5 grains) in 20 per cent. solution, in sterilized oil, or adrenalin (15 to 20 minims) may be used intravenously.

Alcohol requires a special discussion. Briefly I do not consider it a stimulant in the true sense of the word. Viewed from a chemical, pharmacological, or therapeutic standpoint, I think the weight of evidence is against its stimulating properties. It is hard to conceive that this member of the marsh-gas series, all of whose other members—alkanes, alcohols, aldehydes, ketones—are depressant, should furnish this one exception, ethyl alcohol; or two, ethyl alcohol and ethyl ether, which are stimulating. The results of animal experimentation are decided for the depressant effect of alcohol, while I am convinced that the trend of therapeutic opinion is increasingly in the same direction.

That the stimulating effect of alcohol on the mucous membrane of the stomach may reflexly stimulate the circulation is left sub judice; that alcohol has a food value is scarcely denied, and no doubt has contributed to the patient's strength when the food is insufficient; but neither of these effects are justification for the use of alcohol as it has been administered in typhoid fever. In the so-called typhoid state, characterized by cerebral excitation, sleeplessness, rapid pulse, dry skin, coated tongue, and subsultus tendinum, the picture, to my mind, is one of hyperexcitation of the nervous centres by the toxins of the disease. I believe that the improvement seen in this condition by the judicious use of alcohol is due to the sedative effect of the drug on these centres and not to stimulation. This conception confines the use of alcohol to this stage or state of the infection and decries its use where any of the functions are failing from exhaustion. Personally, I would rather not use it at all in typhoid fever, except in the condition just described, and then tentatively: not more than a half ounce of whisky or brandy every four hours.

The urinary tract is not to be neglected. In the early days of the disease especially, the patient's bladder may be overdistended. Close observation should be directed to this organ, and with the first evidences of retention, efforts should be made, by hot applications over the hypogastrium or by hot enemas, to provoke urination. If such measures fail, catheterization must be done, but should be done by the physician, to avoid by his care the infection that so frequently follows this procedure. Overdistention means stagnation, weakening of motility, and lowered resistance to infection by pathogenic organisms and invites a bacilluria. Bacilluria is a very real menace, more to the community than to the patient himself, as true cystitis or pyelitis of typhoid origin is rare. It occurs in nearly 25 per cent. of the cases, often in such numbers as to render the urine turbid. It is most common as the temperature begins to approach the normal and runs into convalescence. It probably arises by infection through the kidney, the bacilli finding a good culture medium in the urine, especially when the urine is of a low acidity and there is any stagnation, such as might result from neglect of overdistention.

The bacilli tend to disappear spontaneously, probably at such a

time as the urine becomes a less favorable medium and the improved tone of the bladder facilitates mechanical removal. However, the condition may remain for weeks, months and, in a few cases, for years. It has been shown that a high degree of acidity, and especially an increasing content of organic acid, inhibit their growth. The effort should be made to eliminate them, as a prophylactic measure, for absence of local symptoms make the convalescent an innocent menace to the community. Urotropin has been shown to have an astonishing effect on their growth, sometimes clearing up a turbid urine in a day or two. It may be given in doses of 5 to 15 grains for two or three days, a week, or continuously, beginning late in the disease and continuing into convalescence.

A good rule would be, beginning when the temperature approaches normal and continuing for a month after, to give 5 to 10 grains of urotropin three times a day for three consecutive days each week. When this does not clear up the bacilli, or a true cystitis prevails, bladder irrigations of silver nitrate, 1 to 5000 daily, or a saturated solution of boric acid, should be instituted.¹

Perhaps the most promising field of specific therapy at this time is the vaccine treatment, the hypodermic use of the dead bodies of the typhoid bacilli, derived from the patient's own blood (autogenous) or from others (heterogenous). The results are not yet sufficiently definite or the details of procedure accurately enough determined to find a place in an article of this kind.

Drugs aimed at the disease itself, intestinal antiseptics, etc., have been left out of consideration, because it is believed that, on the one hand, no good results are to be obtained, while, on the other, harm may be done by the drugs themselves and by the neglect of the more useful measures advised, entailed by reliance on the drugs.

CONVALESCENCE. Convalescence is one of the most trying periods of the disease to deal with, both from the standpoint of the patient and the physician. On the part of the one is the impatience to relieve the gnawing appetite and be released from a confinement which has already dragged itself out to such lengths. On the part of the other is the haunting dread lest the intestinal lesions be not yet healed and that too early activity and too early feeding will induce perforation and establish a relapse.

Less difficulty will be met with in the matter of the dietary if sufficient food has been administered according to my advice, for hunger will be less imperative, and a considerable variety has already been allowed. During convalescence it has been demonstrated that a nitrogen storage takes place which does not obtain in health. We may then add slightly to our protein intake by allowing scraped beef, loin chops, and chicken. The kinds of food that we do avoid, however, are those with a large indigestible residue.

¹ Connell, AMER. JOUR. MED. SCI., May, 1909.

We can feed pretty much as follows, if our patient has been confined largely to a milk diet or has been highly toxic: After the temperature has been normal for four or five days, allow milk toast, then poached egg, then a chop or piece of chicken, then spinach, asparagus tops, purees of peas or tender string beans, the articles of the preceding days being also allowed. Watch the effect of each article carefully.

During the convalescence, excitement must be avoided, business cares excluded, too frequent visits from well-meaning friends interdicted, and other sources of fatigue prevented. After the patient has been restored to a considerable degree of strength, he should still be forbidden to return to work too early. A long vacation, if possible, of three to six months, should be taken, and it is often of great benefit if taken in other surroundings. After the temperature has been normal for a week or ten days, the patient may be propped up in bed, and in three or four days more be allowed to sit up in the chair, a little longer each day, and if all goes well, in a week be allowed to try his feet.

Every case must be approached on its merits, and if the pulse shows by its rate and poor quality that the demands on it are too great, the rest must be prolonged and the getting up be more gradual. To get the patient out in the sun and air is certain to facilitate the progress of his convalescence. During this time his bowels must be attended to with the same care as during his illness in bed, at first aiding with enemas, and later with a mild cathartic like cascara. If there is a great deal of anemia, Bland's pills may be given, 5 grains, three times daily. If the weakness is prolonged, strychnine, $\frac{1}{40}$ grain, three times daily, may be administered.

A slight rise in temperature, day after day, is one of the most nagging features of a convalescence. This may be due to absorption from a neglected bowel, or it may be due to insufficient food, and eminent clinicians long ago pointed out that these patients' temperatures returned to normal when solid food was given them. Others still, who have been highly toxic, whose urea-forming function has been impaired, may become febrile if meat is given too early—the so-called “febris carnis.” Others mend rapidly when kept in the air and light.

PROPHYLAXIS. Typhoid fever is a preventable disease. Its prevention awaits upon the overcoming of an inertia. McCrae divides the subject under three heads: (1) General measures, which are for the protection of the community; (2) special measures in connection with the patient; and (3) preventive inoculation. The knowledge that the disease is conveyed through the water, milk, food, especially oysters and green vegetables eaten raw, demand the supervision of the State and the community, through Boards of Health and Sanitary Commissions, supervision of the water supply, with reference to policing the water sheds, filtration plants, and all the

details dictated by sanitary science. It demands supervision of the milk supply, inspection of the dairies, health of the workers, and a consideration of sewage disposal with reference to oyster beds. It demands notification by physicians to Boards of Health of all cases of typhoid or suspected typhoid fever occurring in a community, and it demands education of the public through schools, lectures, and exhibitions of the part these various factors play in the prevention or spread of the disease.

In connection with the patient arises the question of isolation. Here in New York, as pretty much everywhere else in this country, typhoid fever is treated in the same wards as the general run of cases, and we assume from our familiarity with this condition of affairs that there is no danger in the practice. It is a little startling, then, to be told that the statistics of one of the best conducted hospitals in this country show that from 1.5 per cent. to 2 per cent. of the cases of typhoid fever treated in this hospital are of hospital origin. I have seen this thing occur in my own wards, and so has every attending physician, but still our patients are not isolated. As regards the disinfection of stools, urine, sputum, vomitus, and care of clothing and utensils, all this has been touched upon. If we were faithful in carrying out these measures in every case of typhoid fever, there soon would be no more cases, for, after all, the patient is the true source of typhoid fever.

The attendants about a patient are a source of infections for others unless conscientious in their cleanliness. A great source of danger that might be overlooked are the flies, carrying the infectious material direct on their legs and bodies from the excreta to food and water. Screens are an obvious help in their exclusion.

One great menace to the community, the handling of which is no easy problem, is the chronic bacillus carrier. Some patients harbor for months and years virulent bacilli in the urine, and more commonly in the feces, from constant passage into the bowel of bacilli from an infected gall-bladder. Bacilluria and its treatment have been touched upon. Some day, perhaps, Boards of Health will demand to know whether the stools of a typhoid fever patient are free from bacilli before he is allowed the freedom of the community, as they now demand to know whether the Klebs-Löffler organism is absent from the secretions of diphtheria patients before release from quarantine.

As has been said, serotherapy has not yielded tangible results as yet, but much that is promising has come from the preventive inoculation or vaccination originated and applied to the troops of the British army by Sir A. E. Wright.

The procedure consists in the culture in bouillon of the organism for four weeks, then killing at 60° F. Different strains are mixed together, standardized, and two injections made at intervals of two weeks of amounts of 0.5 to 1.5 c.c., the first containing about

1,000,000,000 bacilli, the second 2,000,000,000. This is usually injected into the flank, from which may result some redness and pain and involvement of lymph glands draining that territory. There may be some constitutional reaction, fever, malaise, nausea and vomiting, but of no significance. Statistics seem to show that among some 20,000 inoculated soldiers the incidence of disease and the mortality was about one-half of that of the 150,000 uninoculated. This looks to be a tremendous advance in the struggle against the disease.

CHOLERA FROM A MODERN STANDPOINT.

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THE recent outbreak of cholera in Europe has furnished reasonable and scientific evidence that the theories we have heretofore entertained regarding the period of incubation of this disease and the character in which it appears have been more or less erroneous. Reliable proof has been presented to show that, while it is probable that typical cases of cholera present themselves within five days after infection, there are mild or irregular cases, the incubation of which may cover a period of weeks, or, as in the case of cholera "carriers," symptoms of the disease may never occur, or when they do, it is usually after the administration of some form of intestinal stimulant sufficiently powerful to arouse the dormant organisms to activity, which is then followed by a sudden appearance of the symptoms of the disease. Even when this does not occur, it is reasonable to believe that carriers who remain apparently well may act as a medium of infection. If I remember correctly, a case of a cholera carrier has already been referred to by Professor Calmette. In this instance a young man, presumably infected in Hamburg during the outbreak of cholera in that city in 1892, traveled for two or three weeks on the Continent, and then, after a night's debauch, suddenly developed the disease.

A similar case has recently occurred in my service at the New York Quarantine Station, the facts of which are as follows: A vessel arrived at Quarantine from Naples after a voyage of fourteen days; the certificate of the ship's surgeon stated there had been no deaths on board, no cases of infectious disease or suspicious cases, nor any case of intestinal trouble during the voyage. None were found sick on the arrival of the vessel. As an extreme measure of precaution at the New York Quarantine Station, during the emerg-

ency above referred to, it was required that a list of all who had applied for treatment of any kind during the transit of the vessel be furnished by the ship's surgeon of all vessels arriving from cholera-infected ports or ports acting as the outlet of infected sections without regard to the character of the ailment. In this instance it was found that six men had applied for treatment for various causes while at sea; none, however, were treated either for diarrhoea or gastro-intestinal trouble of any kind. This group, all of whom were steerage passengers, were not under treatment on arrival, and were practically well. They were transferred to Hoffman Island for further observation. After two days' detention at the latter place, two or three of them were given 2 grains of calomel at bedtime, followed the next day by a cathartic. The following morning one of this group was in a condition of collapse, and died within twenty-four hours afterward. The character of the discharge from the intestinal tract became typical of cholera preceding the death of the patient. The autopsy did not reveal the cause of death. However, the bacteriological examination of the intestinal contents furnished prompt evidence of cholera. Specimens were not only subjected to exhaustive bacteriological investigation by Dr. E. C. Baldwin, bacteriologist of the New York Quarantine Laboratory, but also by Dr. William H. Park, bacteriologist of the Department of Health of the city of New York; and Dr. Anderson, Director of the Hygienic Laboratory of the U. S. Public Health and Marine Service at Washington, D. C., all of whom declared the case to be cholera.

Indisputable evidence has also been furnished that mild and irregular cases of cholera are not uncommon. A case of this character was recently found on a vessel arriving at New York from Italy. The patient was not very ill, and from the history the period of incubation could not have been less than sixteen days.

The fact that a cholera carrier and a mild case of this disease with a prolonged period of incubation occurred on two of the four vessels arriving at the port of New York, would indicate the frequency of these types of cases, and that the popular belief that symptoms of cholera appear within five days after infection is one which cannot be fully accepted.

In view of our present knowledge of cholera, the means by which it is to be dealt with in the future becomes a matter of great importance, particularly to those who are responsible for the public health. In the consideration of this subject it must be fully appreciated that modern quarantine, or the coast defence against the invasion of infectious disease, cannot offer full protection against the introduction of cholera into seaports or the interior. An attempt to carry out such a measure, while it would not secure the desired results, would go far toward destroying commerce, would be impracticable, and not in accord with modern sanitation, chiefly for the

reason that the period of incubation is uncertain, and the existence of cholera carriers has been practically proved. Reasonable and practical quarantine regulations will secure a thorough inspection of passengers and crews on incoming vessels and the detection of infectious diseases if they exist on board either in a mild or typical form, and will also include other valuable means of protection. However, the detention at Quarantine of those who have been exposed to cholera on shipboard, which has hitherto been looked upon as the chief means of preventing the introduction of this disease on this shore, must now be considered only as partial protection, because the assumption that any period represents the maximum time that cholera infection will develop in a person is entirely theoretical, and in view of the fact that long periods of incubation and also cholera carriers, exist. It would seem that the detention of suspects for more than five days, during which time typical cases would probably present themselves, is unreasonable and unjustifiable as a practical method of protection. This brings us to a realization of the fact that hereafter each community must be prepared to accept the responsibility which belongs to it in the protection of its people against this as well as other infectious diseases, and very forcibly suggests what practical sanitarians have long hoped for, that is, the presence in each town and city of a health officer or health officials who are practically and not theoretically familiar with infectious diseases, and who understand the importance of their early detection, either in the typical, mild, or irregular form—an exceedingly important factor in the control of outbreaks. Already, New York, Massachusetts, Pennsylvania, and other States have been working toward the consummation of this important object which in the future must constitute the logical and practical means of preventing the extension of infectious diseases.

Apparently what we have recently learned in regard to cholera would show that our defence against it is much weaker than we have heretofore believed. This is not the fact. There is an extremely optimistic side to this subject and one which has practical and scientific support. The belief has long existed that the ravages that cholera and other infectious diseases have caused in the East is indicative of what would occur if these diseases were to enter any community. This has been the keynote of statements frequently made by alarmists. This belief is without any reasonable or logical foundation whatever, and it may be safely stated that where modern sanitary regulations are in force such conditions will never occur. On the contrary, in the absence of a general infection, cholera does not extend rapidly, and where proper sanitary regulations are in force, should soon disappear. A general infection either on shipboard or on land is a serious and justifiable reflection

on whoever may be in charge of the health of those either on the vessel or in the community where the infection occurs.

During the outbreak of cholera which occurred in Naples in 1882, 800 to 1000 deaths daily was not an unusual occurrence. During the recent outbreak in the same place there has never been more than 20 to 25 deaths during the twenty-four hours, and the outbreak referred to continued only a month before it was officially declared at an end. There are two factors which are accountable for this: First, Naples now has a proper water supply, and no general infection has occurred; and, second, modern sanitary regulations are now enforced in a way which reflect great credit on those in charge of the Municipal Department of Health of that city. Cases of cholera have recently occurred in other European cities—Vienna, etc.—with little or no extension. No more effective or impressive evidence that cholera can be brought promptly under control, and does not extend where even ordinary care is used, is furnished in the case of two vessels which arrived at the New York Quarantine Station during October. On both a case of cholera occurred among the steerage passengers two days after leaving Naples, and death ensued within forty-eight hours. On each of these vessels there were over 1000 steerage passengers, which necessarily involved close and prolonged contact. The cases were suspected by the ship's surgeon, and were promptly removed from the other passengers, and, on their death, were buried at sea. Both vessels were afterward ten days in transit, and on arrival at this station the passengers above referred to were detained for an additional five days, but in neither instance did a secondary case occur. In both cases the disease was contracted before embarkation, and there was an entire absence of any ship infection. If this result can be secured on shipboard, it can also be obtained in a community where modern sanitary methods are in operation. Such evidence must receive the most careful consideration. As a matter of fact, ship infection is now practically a thing of the past. In former times, when sailing vessels, and probably small steamers kept their water supply on the deck, or some place accessible to everyone, there was but little reason why there should not be a general infection on shipboard. However, in modern passenger vessels it would be practically impossible for general infection to occur either in connection with the water supply or food. Neither will general infection follow cholera outbreaks on land if a proper water supply exists, and no community should enjoy the reputation of being under proper sanitary regulations which does not have this. It may be said that the same means of protection which are now employed to prevent general typhoid fever infection would be equally formidable against a general cholera outbreak.

As cholera carriers, mild and irregular cases of this disease may enter a community practically unannounced, it is necessary

that Departments of Health should prepare to deal with such an emergency, particularly at times when there is known to be danger of the introduction of cholera. A rigid investigation should be made of the death certificates which give as the cause of death gastro-enteritis or intestinal trouble of any kind. This should always include a bacteriological examination. Practising physicians should aid in carrying out this means of protection. The effect of this is to secure the early detection of cholera, either in a typical or irregular form, and when this is done, and in the absence of general infection, it is reasonably certain that no serious result will follow, so far as the extension of the disease is concerned.

It would seem reasonable that in the future we must recognize that isolated cases of cholera may appear anywhere which has known or unknown intercourse with the cholera-infected places, and the possibility of this must be recognized; but it must also be understood that while this is so, if general infection is guarded against and proper precautions are taken in individual cases, even the same that are properly carried out in the presence of typhoid fever, we may dismiss the idea of serious results to a community so far as the extension of the disease is concerned.

Bacteriological examination should always be included in determining the presence of cholera. This refers to the examination of alvine discharges or the material taken from the rectum by swabs. At the New York Quarantine Laboratory it has been found that nearly half of the general examinations of this kind, even where there was no clinical evidence or special reason to suspect cholera, showed curved bacilli of various sizes and shapes. In many instances these organisms resembled the cholera vibrios. Where the latter forms are numerous in this examination, the case should be regarded as suspicious until the cultural characters prove it to be otherwise. The presence of a few actively motile organisms in the hanging drop adds considerably to the suspicion.

In cholera carriers and mild cases of this disease the cultures may show the vibrios even though the smear shows very few suspicious organisms. It is usually only in the active cases that the smear and hanging drop, made directly from the discharges or rectal swab, will afford such unmistakable evidence as is required to pronounce the case true cholera from the point of view of the bacteriologist. In all other cases it is necessary to isolate pure cultures and prove them cholera vibrios or otherwise by suitable bacteriological tests.

THE RELATION OF DISEASE OF THE GALL-BLADDER AND BILIARY DUCTS TO THE GASTRIC FUNCTIONS.

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THE effect of certain pathological conditions of the stomach upon the physiological functions of the stomach has engaged the attention of physicians for a number of years. Gastric ulcer, with the associated hyperchlorhydria, is well known. It is only within the past half-decade, or more, that we have begun to realize that a lesion anywhere in the gastro-intestinal tract, or its associated organs, may disturb the gastric functions. We now hear of "acid appendix dyspepsia," of "flatulent gallstone dyspepsia," etc. This has, no doubt, resulted from the very active surgical interference in diseases of the organs of the abdomen, especially of the upper abdomen. The surgeons, among whom are principally Moynihan, Mayo Robson, Paterson, the Mayos, Maurice Richardson, and Deaver, were the first to write of these dyspepsias. My attention was called to this relation some years ago, but more definitely since the meeting of the American Gastro-enterological Association in Boston, where our present presiding officer read a very suggestive paper upon the association of cholelithiasis and hyperchlorhydria.

In looking through the histories of my own cases which bear upon this subject, I have found 249 patients in whom the diagnosis of some disease of the gall-bladder and ducts had been made; and in 258 patients in whom the diagnosis of appendicitis had been made a large percentage had a positive disturbance of the secretory as well as of the motor function of the stomach. In this paper I wish to refer more particularly to the relation between gall-bladder and duct disease to disturbance of the gastric functions, and I shall, therefore, analyze rather closely the 249 cases of gall-bladder and duct affections. In 156 of these cases gastric analyses were made with the usual methods employed clinically to determine the secretory and motor condition of the stomach; 84 (54 per cent.), had a hyperacidity, 31 (20 per cent.) had a subacidity, and 41 (26 per cent.), had a normal secretion. The motor function, so far as could be determined, was normal in about the same per cent. of cases. Of the 249 cases upon which these observations were made, 51 cases came to operation; 30 of these had gastric analyses made; 16 (about 53 per cent.) had a hyperacidity, 8 (about 26 per cent.) had a subacidity, and 6 (about 20 per cent.) had a normal acidity. In a number of the 249 cases the gastric analyses

were made because there were definite symptoms of gastric disturbance associated with the gall-bladder symptoms, but in some it was made because the gastric symptoms were the only ones present, and later, when treatment did not produce the desired results, the abdomen was opened and either gallstones were found, or adhesions from a local peritonitis, due to gall-bladder infection, had occurred between the gall-bladder and duodenum, between the gall-bladder and stomach, or both. In several cases both gallstones and gastric ulcer were found.

	No.	Hyperacid.	Normal.	Hypoacid.
Total gall-bladder cases . . .	249			
Cases with gastric analyses . . .	156	84 (54%)	41 (26%)	31 (20%)
Total cases operated on . . .	51			
Cases with gastric analyses . . .	30	16 (53%)	6 (20%)	8 (26%)

The number of cases upon which these figures are based is, of course, not large, but I have had access to the statistics of other men, and my experience does not seem unusual. My brother, Dr. M. J. Lichty, of Cleveland, gives the following figures. Of 36 gall-bladder and duct cases, 28 had gastric analyses; 19 had a hyperacidity, 5 had a subacidity, and in 4 the secretion was normal.

From these figures it would seem that about 75 per cent. of all gall-bladder cases may be associated with a disturbance of gastric secretion, and of this 75 per cent., two-thirds have hyperchlorhydria. Gastric motility, as well as gastric secretion, was disturbed in about the same proportion of cases. In these days much is said about disturbance of gastric motility and of its relative value clinically compared with gastric secretory disturbances. It is scarcely necessary to draw such distinctions, because the two may frequently be associated in some cases, and, in others one may predominate, while in still others the other predominates. When the statement is made that gastric analyses are misleading, that the motility of the stomach is more important than is the secretory function, it gives evidence that the observer has not made many complete gastric analyses, or that he has misinterpreted his findings.

In presenting these cases, I must necessarily omit a narration of the details of dyspeptic symptoms which pointed to gastric, secretory and motor disturbances, but which are not usually mentioned in text-book descriptions of gall-bladder and duct affections. My main object is to show that certain gastric disturbances are rather constant in these cases, and, if persistent, they may lead one to a diagnosis of the real condition, independently of such pronounced symptoms as jaundice and biliary colic.

Rolleston¹ says: "Indigestion is a frequent result of gallstones;

¹ Disease of the Liver, Gall-bladder, and Bile Ducts.

so-called irregular biliary colic not infrequently manifests itself as dyspepsia, and may be due to adhesions between the gall-bladder and stomach" (or duodenum). But later he says that during the attacks of biliary colic the amount of HCl is either normal or diminished. I think myself, in the height of the attack of biliary colic the secretions may be subnormal, but between the attacks they are more often increased. In some of my cases, repeated examination of the vomitus, during an attack of biliary colic, showed an absence of free HCl and a low total acidity, but the gastric analysis during the interval always showed a hyperchlorhydria. The following case illustrates this well:

Mrs. S., aged twenty-nine years, has had nausea and vomiting for the past five months, but no pain. Four months ago she had a similar attack. A year ago, with such an attack, she had fever, which lasted two weeks and was thought to be typhoid. In the interval the patient had burning and gnawing in the stomach two hours after meals, which was relieved by taking food. Eight years ago the patient had jaundice. At the age of nine years she had a severe attack of typhoid fever. The analysis of the vomitus during the attack for which she consulted me showed no free HCl and a total acidity of only 12. After the attack had subsided, and when she was on her usual diet, an Ewald test breakfast was given and the free HCl was 24, combined 40, and total acid 68. At the operation the gall-bladder was found thick, white, and large, with a stone in the cystic duct. There were no adhesions. The appendix, which was thick, large, and bound down with adhesions, was removed.

It is a matter of observation by many that a patient who has gallstones may give a history of being disturbed in his sleep about 3 A.M., with discomfort or pain in the epigastrium, similar to the discomfort which a patient having a hyperchlorhydria or a so-called nervous dyspepsia experiences.

Moynihan² in an article upon appendix dyspepsia, refers to the occurrence of hyperchlorhydria, or acid dyspepsia, in association with many cases of chronic appendicitis. My experience in over 258 cases of appendicitis, of which, 127 were operated upon and 111 had gastric analyses made, confirms Mr. Moynihan's experience. In the last few years I have called the attention of some of my medical and surgical colleagues to these facts, and all seemed to be of the opinion that there are nearly always rather definite symptoms of gastric disturbances associated with disease of the gall-bladder and ducts, and also with disease of the appendix.

There seems, therefore, a rather uniform opinion that gall-bladder and duct disturbance is associated with symptoms of dyspepsia, such as are usually referred to some disorder of gastric

function. The question now arises, Is there usually a certain demonstrable alteration of gastric function, that is, of secretion and motility, in these cases, and if there is, is it secondary to pathological lesions elsewhere in the gastro-intestinal tract, or is it merely a coincidence?

From the experiments of Pawlow, Starling, Cannon, and Murphy, we can very readily see how a lesion in the gall-bladder and ducts, especially when it has caused local peritoneal adhesions, might produce a pylorospasm and thus disturb both the secretory and motor function of the stomach. It is now generally accepted, especially since Cannon's experiments, that the dominant control of the pylorus lies on the duodenal side of the pylorus, and any disturbance there, such as of the biliary, pancreatic, or duodenal function, may disturb the normally well-balanced mechanism of the pylorus. Cannon and Murphy³ have shown in cats, by an end-to-end anastomosis high in the intestines, that food will leave the stomach only after five or six hours, whereas normally it leaves within ten minutes. Moynihan, in the article on appendix dyspepsia already referred to, suggests that the action of the pylorus as shown by these experiments seems to be protective, and in this way explains the effect of a lesion of the appendix upon gastric function.

I have attempted in the last year or more to determine whether any change in gastric function would occur in dogs in which an artificial lesion of the gall-bladder, corresponding to cholelithiasis in the human subject, had been produced. The primary object of these experiments was not so much to determine specifically the relation of gall-bladder disease to gastric function as to attempt to find a pathological basis, or explanation, for some of the great number of cases of so-called hyperchlorhydria which are now being recognized by both the internist and the surgeon. It seems to have been the tendency, until recently, to look upon patients who have a gastric hypersecretion, but no definite symptoms of gastric or duodenal ulcer, as being simply neurotic and worthy of only scant consideration. I find myself guilty of this error as I review the histories of some cases which had a gastric hypersecretion, for not infrequently have I found these patients (who gave definite symptoms of gastric hypersecretion, and in whom the condition was verified by gastric analyses) suddenly develop definite gallstone or appendix symptoms, and at the operation reveal pathological conditions which must have been the foundation for the whole train of gastric symptoms.

The experiments upon dogs referred to were conducted in the laboratories of the Columbia Hospital with the assistance of Dr. John W. Dixon, assistant surgeon to the hospital, and Dr. Florence Kline, in charge of my private laboratory, to both of whom I wish

³ *Annals of Surgery*, 1906, p. 512.

to acknowledge my indebtedness for surgical and laboratory technique which I had neither the ability nor time to perform myself. We took six healthy dogs of average size and determined as nearly as possible their normal gastric function after a test meal similar to the Ewald test breakfast usually employed clinically. Gastric secretion, as well as motility, was observed as nearly as possible as it is in man. The technique was as follows: Two ounces of bread was thoroughly dried and broken into small pieces and soaked in eight ounces of water, so as to make an emulsion which could be easily injected through a stomach tube. A dog, after having fasted for ten or twelve hours, was given this portion through a stomach tube which had been passed into the stomach. At the end of thirty or forty minutes the stomach was aspirated by inserting the stomach tube with a politzer bag attached. The contents thus recovered was filtered and the acidity estimated by titrating with a decinormal sodium hydroxide solution.

A number of tests were made in this way until the results became rather constant, or until a fairly definite average was obtained. At a sufficient time after the dog became accustomed to his new surroundings, and also to the passing of the tube to determine his individual acidity and motility, the abdomen was opened under anesthesia and a foreign body, usually a hard cinder from the furnace room, which had previously been dipped into a culture containing streptococci, or mixed microorganisms, was inserted into the gall-bladder, which was opened and again carefully closed and returned into the abdominal cavity. After the dog had recovered from the immediate effects of the operation and was again upon a general diet, the analyses of the stomach contents were resumed, and, after a certain time, a comparison made between the gastric analyses before and after the operation. Five dogs were operated upon and foreign bodies inserted into the gall-bladder, the sixth being kept as a control.

Dog No. 2, after having twenty-three test breakfasts given in the course of thirty-one days, showed an average acidity represented by 23.7, and was operated upon, under ether anesthesia, January 19, 1910. The gall-bladder was delivered through a Kocher's incision, opened, and a rough cinder the size of a pecan was inserted. The gall-bladder was closed and returned to the abdominal cavity. Recovery was satisfactory. On January 25, when the dog was taking his usual diet, the test breakfasts were resumed. It was very soon found that the stomach did not empty as promptly as before the operation. In sixty-five days twenty-seven test breakfasts were given, showing an average total acidity of 28, or a gain of 4.6 points. On March 25, 1910, the abdominal cavity was again opened for the purpose of producing a lesion at the cecal pouch (appendix). The gall-bladder was found very much shrunk and tucked up as far beneath the liver as possible.

Dog No. 4 had thirty-two test meals in forty-three days, with an average acidity of 21. Was operated upon, February 9, 1910. A cinder, which had previously been dipped into a culture of streptococci, was inserted into the gall-bladder with the usual technique. In the course of sixty days twenty test breakfasts were given, with an average acidity of 19. On April 1, 1910, the abdomen was opened, and a few firm adhesions were found binding the omentum to the gall-bladder.

Dog No. 5, after twenty test meals in twenty-eight days, showed an average acidity of 22.8. Was operated upon, February 10, 1910. A cinder infected from a mixed culture was inserted into the gall-bladder. Following the operation the wound in the abdominal wall was opened and there was a marked local infection, which, however, finally granulated over nicely. After the dog had entirely recovered from the operation, twenty-four test meals were given in sixty-three days, with an average acidity of 33.3. On April 15, 1910, an exploratory abdominal operation was done, and extensive adhesions were found between the gall-bladder, omentum, and abdominal wall.

Dog No. 6 had thirty-one test meals in forty-one days, with an average total acidity of 21.8. Was operated upon, March 18, 1910, and a cinder infected with pus from a patient having puerperal septicemia was inserted into the gall-bladder. The incision healed without any infection. After recovery from the operation twenty-five test meals were given in sixty-eight days, with an average total acidity of 24.5.

Dog No. 7 had fourteen test meals in fifteen days, with an average total acidity of 24.6. Operated on February 25, 1910, and a cinder infected from a streptococcus culture was inserted into the gall-bladder; the wound closed without any infection. After the operation twenty-one test meals were given in fifty-nine days, with an average total acidity of 37.5, or an increase of 13 points. On April 22 the abdomen was again opened for the purpose of examining the gall-bladder and producing a lesion in the appendiceal pouch. The gall-bladder was very small and high under the liver. It was bound down by a great many tense bands of adhesions.

The average results of the analyses of the gastric secretion are as follows:

	Before operation.			After gall-bladder operation.		
	Test meals.	Days.	Average acidity.	Test meals.	Days.	Average acidity.
Dog No. 2	23	31	23.7	27	65	28.0
Dog No. 4	32	43	21.0	20	60	19.0
Dog No. 5	20	28	22.8	24	63	33.3
Dog No. 6	31	41	21.8	25	68	24.5
Dog No. 7	14	15	24.6	21	59	37.6
Dog No. 8	24	58	16.7			

It will be seen that in Dogs Nos. 2, 5, and 7 considerable change in the gastric secretion took place. The motility also was disturbed. When these experiments were begun, it was intended to aspirate the stomach an hour after the test meals had been given, as is done clinically, but we soon learned that the gastric motility in the dog was more rapid than in man; we, therefore, withdrew the contents in thirty minutes, and even then sometimes did not obtain a satisfactory amount. After the gall-bladder operations this was suddenly changed, and at the end of thirty and even forty and fifty minutes abundant amounts could be aspirated. This change was so evident and constant that we concluded the motility of the dog's stomach was decidedly disturbed as the result of the pathological conditions which the foreign body in the gall-bladder had produced. The change, or delay, in motility seemed to be in direct proportion to the extent of the lesions produced.

It seemed to us with this technique we were able to produce conditions and determine results in the dog very nearly as they are found clinically, and that we had, as nearly as possible, met the necessary requirements for conducting an experiment. We, of course, appreciate that the Ewald test breakfast does not give us scientifically correct information of gastric function, and yet it is the method generally employed clinically. The Pawlow artificial second stomach pouch, or cul-de-sac, was not employed in these experiments, because we were of the opinion that a disturbance of the normal gastric secretion and motility would be caused by the operation itself and the consequent adhesions. We hope to confirm this opinion by experiments which are now being conducted in our laboratory.

Our technique might be objected to on the ground that a meal forcibly injected into a dog's stomach would not excite the amount of secretion or degree of motility occurring after a meal which the dog had taken with his proverbial relish and greed. But the object of the experiment was not so much to determine the normal gastric secretion in dogs as to determine whether the constant secretion and motility found by a certain technique would be disturbed by producing a lesion in the gall-bladder and ducts.

We attempted to check up our experiments by having a sixth dog as control in the same kennel with the dogs which had been operated upon, whose stomach contents were examined every few days, but who was not subjected to operation. We very soon learned that a number of factors, such as irregularity of feeding, disturbance of health and comfort, segregation of the dogs, and the introduction of a keeper who was not agreeable to them, influenced gastric secretion quite decidedly, but we attempted in every way possible to obviate these factors, and we feel that our results are as reliable, if not more so, than those obtained clinically.

I feel, therefore, inasmuch as my own clinical experience, together

with that of the large experience of other clinicians, seems to be confirmed by the experimental evidence which I have attempted to present, that I might safely draw the following conclusions:

1. A lesion of the gall-bladder and ducts may disturb the gastric functions.

2. This disturbance most frequently consists of a hypersecretion of gastric juice and a diminution of gastric motility, and may be in direct proportion to the lesions present.

3. So-called hyperchlorhydria, with its accompanying symptoms, should be looked upon as an evidence of some definite pathological lesion somewhere in the gastro-intestinal tract or its appendages, and should be treated symptomatically only when organic disease can be excluded with a satisfactory degree of certainty.

THE DYSPEPSIA OF OLD AGE.

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For a number of years certain digestive disorders in old people have come under my observation, and in these the cause, seemed purely dependent on the changes incident to advanced years. The manifestations of senility shown by atheromas, degenerations, ossifications, calcifications, etc., have been discussed at length by contemporary medical writers, but some of the strictly gastro-intestinal disturbances have received scant notice, being regarded more as pathological features of maturity than normal accompaniments of old age. Gerontology we find laid down already, and Dr. Nascher, of New York, recently suggested the term geriatrics to cover the same field in old age that pediatrics covers in childhood.

It may be of interest, therefore, to consider some of the dyspepsias of this advanced period of life as radically different from those occurring during the height of adult vigor, while normal metabolism should be waging an equal warfare between the constructive and destructive forces. According to Fenwick's investigations, out of every 100 cases of chronic dyspepsia in persons over sixty-five years of age, 66 are secondary to organic diseases of some important organs of the body, while 34 owe their symptoms to a progressive degeneration of the secretory structures of the stomach and intestines.

The stress of over sixty-five years of bodily activity will, in a majority of cases (at least two-thirds), result in disease of either the kidneys, prostate, heart, lungs, liver, pancreas, or a chronic gouty condition, which will set up a chronic asthenic gastritis; while in a

fair proportion of this number (possibly 10 per cent.) the dyspepsia dates back to long-continued hypersecretion due to gastric or duodenal ulcer, gallstones, or a diseased appendix. In the remaining one-third—those to whom this study principally applies—no marked organic impairment can be located, but the general assimilative powers decline, the body assimilates less organic matter, and destroys less inorganic matter, bringing about a waste of tissue and an increase of salts. Even should there be no general arteriosclerosis, abdominal arteriosclerosis may be present, giving rise to ill-defined digestive disorders, angina, and epigastric discomfort. Again, there are certain obscure dyspepsias, in which the arteriosclerosis is probably confined to the intestines, and in which such diagnoses can be made only by exclusion, the main indication, however, being that the gastro-intestinal disturbances are not dependent so much on the quality of the food as on the quantity.

Admitting that our information concerning these senile dyspepsias is in a somewhat chaotic state, it would seem permissible, and perhaps helpful, to divide them into two classes, which will be readily recognized clinically. These classes may be termed the *hyperkoric* and the *akoric*.

In the first, or hyperkoric cases, the degeneration and insufficiency of the digestive organs simply keep pace with the rest of the body. With decreased muscular activity there are decreased assimilative powers, and the patient finds that articles of food now disagree which were formerly digested with ease.

I have in mind at present a gentleman, now deceased, who informed me that up to sixty years of age he hardly knew he had a stomach. Possessing the appetite of a cormorant and the digestion of a rhinoceros, he was much surprised when suddenly, following neither illness nor change in habits, he realized that his appetite was diminishing, and that if he ate more than it dictated he would suffer. This hyperkoria completely revolutionized the last fifteen years of his life. He was apparently a hale old man, few of his daily habits except those of eating being changed, but he learned by several painful experiences that his digestive capacity had become curtailed, and for the rest of his life, which was terminated by an acute dysentery, he ate only about one-fourth of the amount formerly required. The only clinical symptoms I could ever elicit in this interesting case were intermittent tenderness over the abdominal aorta and occasional epigastric pulsation.

A large proportion of persons over fifty years of age show a diminution of free hydrochloric acid; a test meal revealing hydrochloric acid content as high as 25 becomes a decided exception, unless the oxyntic cells are subjected to some constant irritant. Pawlow tells us that the hydrochloric acid as poured out by the peptic glands is of a constant percentage value, by which he means that in each individual each gland secretes a juice possessing the same degree of

acidity, never varying. Admitting this, the gross findings would indicate a diminution in quantity of gastric juice, probably shared in by all the other intestinal juices. Thus we have different degrees of hypoacidity reaching to complete achylia gastrica. When this condition obtains the sense of hunger and thirst are wisely obtunded; the palate no longer beckons to gastronomic delights; the olfactories, once the psychic outposts of the digestive system, cease their agreeable suggestions; the digestive glands respond but tardily to the secretagogues, which formerly incited such joyous action; while the "appetite juices" well up but lazily from their tiny fountains. It is then that the old man realizes what Solomon meant, when, in describing old age, he wrote "desire shall fail," and the hungry tramp with his gnawing stomach becomes an object of real envy.

The hyperkoria, or early sense of satiety, is Nature's protection, and the dyspeptic manifestations simply indicate that the digestive machinery is performing its tasks haltingly and imperfectly. The machinery itself may be intact, but the dissolving and transforming juices are too scanty for efficient work.

The second class, or akoric dyspepsia, is generally found in obese old people, or in those in whom the mental edge, perhaps once sharp and bright, has been either blunted or worn off. There is more than habit in obesity, and the lessening activity is not so much the cause as the result of it. It is not lack of exercise that induces the corpulence of advancing years, nor is a morbid appetite an indication of renewed vigor. Both are evidences of declining vitality, and of the failure of that steady poise of maturity, that competent metabolic adjustment, so aptly termed by Herbert Spencer "the moving equilibrium." Assimilation no longer equals its calls; the departments of construction and repair are not now aggressive, and the task is to keep what has been won. The normal tonicity of the stomach gives place to relaxation, its walls become flabby, and more food is required to give the sensation of comfortable fullness. Pyloric insufficiency is generally present, while atonic constipation supervenes almost as a matter of course. Under such circumstances the lot of the aged sufferer is sad. Hunger cannot be satisfied, elimination is imperfect, and the intestines veer between obstinate constipation and lenteric diarrhoea.

There came recently under my observation an instance of this sort—a gentleman, highly educated, and at one time a prominent man of affairs. Having retired from business, he purposed spending his declining years in ease and quietude, and all went well until his family noted the development of an insatiable appetite, coupled with a slight dulling of his mental faculties. Although over seventy-five years of age, he showed no marked organic change, except a dilated stomach, and I was forced to the diagnosis of a senile akoric dyspepsia, with probable intestinal arteriosclerosis.

Apart from the lenteries so frequent in this class of cases, there

is often the mitigating presence of a compensatory diarrhœa, which comes on at regular intervals, washing out the stagnated products of katabolism, and with each visitation affording a new lease on life.

The management of these two classes of senile dyspepsia naturally differs. In the hyperkoric dyspepsia we generally find that the food ingested furnishes barely enough calories for daily existence, allowing none for repair or "lost motion." So many articles have disagreed in the past that there is frequently a sitophobia, or fear of food, so that in many cases insufficient nourishment indirectly hastens the senile decay.

As physical activity increases combustion and waste, active exercise should be limited. The food should contain a minimum of non-digestible, non-nutritious elements and lime salts. Most of the predigested foods on the market are unavailable on account of their high percentage of alcohol, but the meat juices, peptonized milk, malted milk, lactone buttermilk, malt extracts, eggs, and the farinaceous foods may usually be given, to which, if deemed advisable, the gastric and pancreatic ferments may be added. The proportion of cellulose, which should properly enter into the dietary of adults so as to promote peristaltic activity, may be omitted from consideration, and all foods should be given in the most concentrated form, and in the shape most easily assimilated.

The principles of physiological economy, so carelessly followed during the period of anabolic excess, must now be rigidly observed; like the man whose earning capacity being diminished, has to adapt his methods of living to a depleted income, so constant care should be exercised, on the one hand, not to overtax the enfeebled digestive powers, and on the other hand, to avoid the pitfalls of caloric bankruptcy.

The management of the akoric type of senile dyspepsia will call for infinite tact and discretion. To curb the cravings of a second childhood, to regulate wisely an imperious will, untempered by judgment, to appease the gnawings of a constant bulimia, without overwhelming the intestines with undigested food, will demand a study of each individual. Should the teeth be bad, or mastication imperfect, soft or previously comminuted food will be advisable, and the aching gastric void may be at least partly filled with liberal potations of weak tea, or hot water flavored with sugar and milk. Between meals chewing gum will frequently assuage the pangs of hunger, and, unless there are esthetic objections, it may be indulged in ad libitum.

Alcohol has but little place in these conditions, either hyperkoric or akoric, and the remarkable instances of youthful old people, sustained and soothed by certain brands of whisky, and so graphically portrayed in the secular press, are generally the perfervid productions of paid advertisement writers. Cathartics should be used with caution, and gentle methods for cleansing the bowels should be combined with measures to overcome subsequent weakness.

The treatment of incidental complications need not be touched here. These complications are rarely avoidable, and often end the scene very quickly. In the department of the bodily upkeep, senile changes may be retarded, but their progress is sure, their termination fixed.

The only human agent on record who ever stopped the flight of time was Joshua, and even he did not turn back the clock. So, while we cannot administer from a spoon the elixir of youth, we can in many ways aid our timeworn patients in the task of growing old both gracefully and comfortably.

THE DIAGNOSIS OF TUBERCULOSIS OF THE BRONCHIAL GLANDS.

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IN view of the fact that pulmonary tuberculosis is almost always secondary to tuberculosis of the bronchial glands, and as we know that months, even years, may elapse before the lung becomes involved, it is surprising that the diagnosis of bronchial gland tuberculosis has not received more attention. Except for a short paper, presented by Gray,¹ two years ago, which dealt chiefly with vertebral bronchophony, the subject has never been discussed by the National Association for the Study and Prevention of Tuberculosis; nor was it considered at the recent International Congress of Tuberculosis. Yet disease of the glands frequently gives symptoms, and often physical signs, months before the lung is invaded.

The lymph nodes, known as the tracheobronchial or mediastinal glands, are divided into three groups. The tracheal glands, which surround the trachea, are in relation with the superior vena cava, and the pneumogastric and recurrent laryngeal nerves. The group situated at the bifurcation of the trachea, are in contact with the pneumogastric nerve, and also with the pericardium anteriorly, and the œsophagus posteriorly. The pulmonary vessels are below, and the spinal column, adjacent vessels, and nerves on the right. The hilum glands extend along the bronchi to the lungs, and are in relation with the branches of the bronchial and pulmonary vessels.

The glands at the bifurcation of the trachea are usually the first to be diseased, Wollstein² finding the gland adjacent to the right bronchus the seat of the primary lesion in 74 per cent. of her cases.

¹ Proc. Nat. Assoc. for Study and Prevent. of Tuberculosis, 1908, p. 300.

² Arch. Int. Med., 1909, No. 4.

The individual glands rarely exceed an inch in diameter, and are usually smaller. As the trachea extends downward, it inclines to the right, so that at its bifurcation at the level of the fourth or fifth dorsal vertebra, it is near the right border of the vertebral column.

It is unnecessary in this paper to take up the pathology of tuberculous glands. It suffices to state that they may harbor tubercle bacilli when there is neither macroscopic nor microscopic evidence of their presence. The bacilli may remain for a time in a dormant, or so-called "lymphoid state."

The bronchial glands are much more prone to caseous degeneration than the cervical or mesenteric, in which the lymphoid state is often of long duration. When the process subsides, the glands frequently become calcareous.

SYMPTOMS. The onset is usually insidious, Schossman³ stating that "the lack of cause for the change in the general condition of the child is truly characteristic of tuberculosis of the bronchial lymph nodes."

The symptoms are in part due to the absorption of the toxins of the tubercle bacilli, and also to the pressure of the glands upon vascular, bronchial, and nervous tissues. The toxic symptoms are familiar to us all. They are poor or capricious appetite, fatigue, especially in the morning, languor, irritability of temper, and irregular pyrexia. Dautwiz⁴ in his exhaustive monograph on bronchial gland tuberculosis, mentions as an early symptom pain of indefinite origin, felt within the chest, which is brought on by deep breathing or vigorous physical exercise. Sometimes there is a substernal pain. Krämer⁵ speaks of a constant pain in the mammary region, associated with interscapular dulness, both of which disappear under tuberculin treatment. Huskiness of the voice may be present. Schick⁶ has called attention to the expiratory stridor of infants with enlarged bronchial glands. This resembles somewhat the expiration of asthma, but differs in that it is more often constant than paroxysmal. This sign, which is rarely present after the fourth year, is usually preceded by a few weeks of coughing, commonly diagnosticated bronchitis. When the child is resting quietly one observes that the stridor occupies the whole of expiration. Following excitement or a hard coughing spell the respirations may be normal for a time. In advanced cases the breathing becomes labored as the stenosis increases. These severe forms have been mistaken for laryngeal croup, and intubation has even been performed. This mistake can be avoided if one remembers that the voice is lost in diphtheria but not in bronchial gland enlargement. Under the term "status lymphaticus,"

* Diseases of Children, 1908, ii, 603.

Beitr. z. klin. d. Tuberkulos, 1909, xiv, 335.

* Beiheft z. med. Klin., 1908, iv, No. 9.

* Wien. klin. Woch., 1910, xxiii, 153

Friedländer⁷ and Rachford⁸ have reported cases whose clinical histories are quite typical of tracheobronchial adenopathy. In Friedländer's case the stridor was inspiratory. Most of the infants whom Schick observed with expiratory stridor died subsequently of tuberculosis.

Eventually a cough begins, and it is because of this symptom that medical advice is usually sought. The typical cough is paroxysmal, "brassy," and quite characteristic. While it often suggests the cough of pertussis, it is not always so severe. I have heard it when it suggested a cavity in the lung. It is of reflex origin, depending upon the pressure of the swollen glands on the vagus nerve. As there appears to be no explanation as to how this reflex takes place, the following hypothesis is suggested:

Cough is usually incited by the stimulation of the terminal filaments of the superior laryngeal nerve, a branch of the vagus, which ramifies in the mucous membrane of the larynx. The vagus is not a sensory nerve below its superior laryngeal branch. MacKenzie⁹ has shown that a long-continued stimulation may set up a condition of irritability or hypersensitiveness in nerve centres. It is possible that such a condition of irritability is brought about in the ganglion of the vagus trunk by the pressure of the glands, and that as a result the superior laryngeal nerve, which arises from the inferior ganglion of the vagus, is stimulated, and a cough results. This hypothesis would explain the cough of pleurisy, and the tickling in the throat complained of by nearly all incipient cases of tuberculosis. It is possible that the cough of pertussis is occasioned in like manner.

Long-continued pressure may cause erosion of the trachea or bronchi, and the aspiration of the ruptured gland may be followed by a pulmonary lesion.¹⁰ The œsophagus may in like manner be invaded, and fatal hemorrhages have resulted from the erosion of bloodvessels when the lungs have been free from disease.

Fisher¹¹ reports the case of a boy, aged five years, who died from this cause, and Barry¹² tells of the death of a woman, aged seventy-one years, whose caseous bronchial gland had caused a rupture of the vena cava. At the autopsy of a man, aged twenty-eight years, who died with symptoms of hemorrhage, Griffin¹³ found in addition to a pleurisy with effusion, intense congestion of the trachea at its bifurcation, and an enlarged and caseous bronchial gland surrounded by a coagulum the size of an English walnut. The pretracheal glands were moderately enlarged, necrotic, and the seat of numerous hemorrhages.

⁷ *Archiv. Pediatrics*, 1907, xxiv, 490.

⁸ *AMER. JOUR. MED. SCI.*, 1910, cxi, 550.

⁹ *Symptoms and their Interpretation*, 1909, Chapters iii, iv, v.

¹⁰ Hall, *AMER. JOUR. MED. SCI.*, 1899, cxviii, 185, has reported a case in which a large piece of the bronchial gland was coughed up, with relief of symptoms.

¹¹ *Lancet*, 1909, i, 28.

¹² *Med. News*, 1885, xlvii, 236.

¹³ *Med. Rec.*, 1891, xxxix, 166.

Another patient of Fisher's,¹⁴ a girl, aged seven years, who was in good health, and in whom there was nothing to suggest pulmonary tuberculosis, spat up blood from time to time for over three years.

It seemed desirable to ascertain the reliability of a number of signs said to be indicative of tuberculosis of the endothoracic glands. To this end 175 children have been studied; the results in each instance were compared with the skin tuberculin test—the undiluted “old” tuberculin being used. Some of the children had entered the Hartford Hospital for operation for adenoids and hypertrophied tonsils, and through the courtesy of Dr. Frederick R. Crossfield, I was permitted to examine them. I am indebted to Dr. Albert R. Keith for the opportunity of studying a number of the children at the Hartford Orphan Asylum. The remaining cases were scholars at our Preventorium, or Outdoor School.

INSPECTION. We observe in the first place, that the child with tuberculosis of the bronchial glands is usually frail, but this is not always the case, and Dautwiz very truly says that the condition “may hide back of the rosy cheeks of a happy, contented child, who is kept in good physical condition.”

Seventy-seven out of 146 of our children in whom the appearance was recorded, were noted as being frail, and of these 57 per cent. reacted to tuberculin; 69 children who were not so classified, but included the robust and “indifferent,” were tested, and 32 per cent. reacted; 59 children positive to tuberculin, who were weighed, were on the average twelve pounds under weight for their ages.

One should next look for the presence of dilated veins over the anterior aspect of the thorax. These veins were present in 92 out of 173 cases in this series, 50 per cent. of whom reacted to tuberculin. The presence of dilated capillaries in the region of the seventh cervical vertebra seems to be a sign of less value. Slight puffiness of the face and eyelids from venous obstruction may be present.

One sometimes observes slight inequality in the expansion at the apices. This is best detected by looking down over the anterior aspect of the chest while standing behind the patient. There may even be slight retraction without disease of the apex. This I have proved by radiograms. The movements of the Adam's apple should be noted, as de la Camp¹⁵ has observed that in some cases with enlarged thoracic glands, it is stationary instead of descending with inspiration.

PALPATION. It would seem that palpation affords us the most reliable means of differentiating between active and inactive gland disease. Tenderness over the manubrium sterni and at the sterno-

¹⁴ Loc. cit.

¹⁵ *Ergebnis. d. inn. Med. u. Kinderheil*, 1908, i, 556.

costal junction is suggestive of bronchial adenopathy, but these tender areas occur less frequently than tenderness over the spines of the upper thoracic vertebræ. This was first described by Petruschky¹⁶ some years ago, and other clinicians have since attested its value. It is best elicited as follows:

The examiner is seated, and the child with arms crossed, stands sideways between his knees, in order that the expression of the face may be noted. Then, without explaining what is to be done, firm pressure is made over the vertebral spines. The change of facial expression is the best indication of spinalgia, though in some instances sudden approximation of the scapulæ takes place when the tender spines are palpated. No tenderness being elicited by this means, it is then permissible to ask if all the spines feel just alike, and a repetition of the test may reveal a less marked tenderness. One should make firm pressure of the vertebral spines, going from above downward, and marking any tender spots; then begin in the lumbar region and go upward. The tenderness at times is extremely acute. It seems to be most often present over the fifth thoracic vertebra, though it is not uncommon to find spinalgia over several of the upper thoracic spines.

Petruschky does not explain what it is due to. He suggests that it may be caused by a periosteal irritation, the result of disturbances of circulation, or to the presence of minute tuberculous foci in the spinal column.

One should remember that MacKenzie has noted tenderness over the upper four thoracic spines in diseases of the heart, and over the fourth, fifth, sixth, seventh, eighth and thoracic vertebræ in stomach lesions. He, too, is unable to explain it. Inasmuch as all these viscera are supplied by the vagus, it would seem as though it were a reflex pain, but just how it takes place is not clear. The spinal tenderness of hysteria and neurasthenia is not limited to the upper thoracic vertebræ.

It is very likely that the backache in the interscapular region, so often complained of in early stages of tuberculosis, is due to tuberculous glands.

Petruschky reports 79 cases of spinalgia, 77 of which reacted to tuberculin. Advanced cases of tuberculosis do not present this phenomenon. The sign was present in 23 out of 58 children of my series; and 83 per cent. of them reacted. Ten adults recently examined, in whom there was a strong suspicion of an early lesion, had spinalgia; 80 per cent. of them reacted to tuberculin. In both children and adults with toxic symptoms this sign was rarely absent. It has been observed that both rest in bed and the therapeutic use of tuberculin cause a disappearance of the spinal tenderness.

Neisser¹⁷ has developed an ingenious method of palpation, which however, is not practical in children. He covers the end of a small stomach tube with a condom, and after introducing it, 25 c.c. to 26 c.c. from the teeth, inflates it through the tube. As the condom becomes distended, it presses on the glands, producing the characteristic pain between the shoulder blades. A number of observers have found this sign present in a large percentage of cases.

PERCUSSION. The detection of dulness over the manubrium sternum has little diagnostic value. Up to about the sixth year the thymus give a dull note, as a rule. The left lobe, which extends higher than the right, can frequently be detected to the left of the sternum in the first interspace. According to Dautwiz, the thymus may persist to the thirteenth or fourteenth year. Then, too, so many other structures intervene between the sternum and bronchial glands that manubrial percussion is of little value. Bing¹⁸ believes, however, that with *very light* percussion over the right half of the manubrium sterni, he can elicit slight dulness when there is glandular enlargement. Dulness over the sternum, or in the inner third of the first left interspace was present in 41 of our cases, 49 per cent. of whom reacted to tuberculin.

Parasternal dulness in the second and third interspaces, caused by enlarged hilum glands, was not sought for in this series of cases. It is possible that the dulness occasionally present in the second and third interspaces on the right, in the parasternal line with right apical disease, is caused by enlarged bronchial glands rather than by an increase of cardiac dulness (to which it is commonly attributed) from the retraction of the anterior border of the right lung caused by cicatrization at the apex. Though, as a rule, little is gained by percussion anteriorly, information of real value may be obtained by posterior percussion. Notwithstanding that spinal percussion was mentioned by Auenbrugger¹⁹ it has never been extensively practiced. Advocated by Ewart,²⁰ and von Koranyi²¹ and recently by De Costa,²² it was de la Camp who made an extensive investigation of its value in the diagnosis of enlarged bronchial glands.

Without going into the elaborate studies of Koranyi, and Ewart, it is sufficient to state that a dull note is obtained normally over the upper four thoracic vertebræ, and that over the remaining

¹⁷ Deut. Arch. f. klin. Med., 1905, No. 86, quoted by Nagel, Jahrb. f. Kinderh., 1908, lxxviii, 46.

¹⁸ According to Quain, quoted by Hall, Phila. Med. Jour., 1900, vi, 1059, manubrial dulness from bronchial glands can sometimes be obtained, if one percusses at the end of a forced expiration, with the head in dorsal flexion.

¹⁹ Camac, Epoch-making Contributions to Medicine, Surgery, and the Allied Sciences, p. 125.

²⁰ Lancet, 1899, ii, 261.

²¹ Handb. d. spec. Path. u. Therap., 1897, iv, 717, quoted by de la Camp (q. v.).

²² AMER. JOUR. MED. SCI., 1909, cxxviii, 815.

dorsal spines the note is a combination of osteal and pulmonary resonance. Dulness over the fifth or sixth dorsal spine is pathological, and is indicative of mediastinal tumor. Ewart states that the fifth spine is normally dull. This does not agree with my observations.

De la Camp attaches great importance to this dulness, and though he found it in only one-third of his cases of enlarged glands, it was in some instances the only sign of their presence. He suggests that percussion at the end of expiration may elicit slight dulness, otherwise not demonstrable. Nagel ascertained by experiments on cadavers, that 10 c.c. of wax injected anterior to the fifth dorsal vertebra would not produce dulness, but that 15 c.c. so injected would. He believes, that the dulness is not so much due to the glands per se as to the lessening of pulmonary resonance, from the pushing aside of the lung by the glands. Percussion of the vertebral spines was performed in only a small number of our cases. It was found at or below the fifth dorsal spines in 9 out of 40 children who were positive to tuberculin; 7 adults, all of whom had other signs of bronchial gland enlargement, had either vertebral or paravertebral dulness.

Krämer considers spinal percussion greatly inferior to paravertebral percussion. He is convinced by his investigations that if one have a true ear and percuss with sufficient delicacy, slight degrees of dulness can be detected whenever there is glandular enlargement. The dulness may or may not merge into apical dulness when the apex is involved. The dulness may be bilateral or unilateral, and when the former, the area of impaired resonance is usually unequal. Krämer attributes the dulness largely to the engorgement of the blood and lymph vessels, due to the glandular pressure. He believes, that the initial dose of tuberculin should be governed by the size of the area of dulness: the more extensive the dulness, the smaller should be the dose. As in all cases in which delicate percussion is employed, more trustworthy results are obtained if the eyes are closed and a dermatographic pencil used. The sense of resistance is perhaps as significant as the impaired resonance. Paravertebral percussion was carried out in too few cases in this series to draw deductions, but in the cases in which it was detected other signs of bronchial glandular enlargement were present. The dulness at the right apex, which is sometimes present without disease of the lung, and attributed by Krönig to nasal obstruction from adenoids, is believed by Bing²³ to be due to enlarged bronchial glands, which tend to be arranged more in groups on the right than on the left side.

AUSCULTATION. Like vertebral percussion, auscultation over the vertebral column has never been widely employed. A few years ago d'Espine²⁴ called attention to the fact that enlargement of

²³ Ugesk. f. Laeger., 1910, lxxii, 199.

²⁴ Bull. acad. de méd., 1907, lvii, 167.

the endothoracic glands gave auscultatory signs that were quite distinctive. In the normal individual the tracheal quality of the respiratory murmur ceases at the seventh cervical vertebra. When the bronchial glands are enlarged, however, the tracheal quality, somewhat diminished in intensity, is continued downward over the thoracic spines for a variable distance. In some instances the bronchial character is absent over the upper thoracic vertebræ, but present at the fifth, and possibly below. Except in the extremely emaciated one can place the bell of the stethoscope directly over the vertebræ. The character of the voice, especially the whispered voice, affords the most reliable evidence upon which to base a diagnosis of enlarged tracheobronchial glands. The words three thirty-three being repeated slowly, when glandular enlargement is present, bronchophony is quite distinct. If one listens with care, it will be observed in most cases that the final "e" of the last word "three" is heard for an appreciable time after the voice stops. Gray refers to it as the "postphonal quality." This is normally present over the trachea. It may be heard over the upper thoracic vertebræ, or only at the level of the fifth dorsal. I have heard it as low as the eighth dorsal.²⁵ The split syllable, referred to by Gray, was not observed.

As a rule, the bronchial quality is lost when the stethoscope is moved to either side of the vertebral column, but in some cases it is heard as distinctly at one side, rarely at both, as over the spines. In one instance, the whispered voice was so marked as to suggest a cavity at the apex of the left lower lobe. Flexing the head intensifies the bronchophony.

No infants are included in the cases herewith reported, but the sign is of equal, perhaps of greater value than in older children, as the signs of pulmonary involvement in infants are notoriously indefinite. In these little ones the character of the cry and of expiration must be substituted for the spoken words.

Vertebral bronchophony was present in 80 out of 168 children, and 66 per cent. of those in whom it was detected reacted to tuberculin. Those not giving the sign, gave 28 per cent. of positive reactions; 44 out of 80 frail children had vertebral bronchophony, and 70 per cent. of these were positive to tuberculin; 39 of the 80 in whom the sign was negative, reacted to tuberculin; 24 adults who had spinal bronchophony, gave 80 per cent. of positive reactions. I have recently had autopsy confirmation of the value of this sign. The necropsy upon a woman, aged sixty-one years, who had had vertebral bronchophony over the upper four cervical vertebræ and slightly prolonged expiration at the right apex posteriorly, revealed

²⁵ In an adult recently examined in whom the clinical diagnosis of enlarged bronchial glands was substantiated by a radiogram, vertebral bronchophony extended to the second lumbar vertebra.

a mass of partly caseous glands about an inch in diameter lying in the angle formed by the trachea and the right bronchus. The infra-tracheal glands were but slightly enlarged and the right apex showed no signs of infiltration. D'Espine reports several similar cases.

It is of interest to note that Laennec²⁶ detected this interscapular bronchophony. He says, "In persons, however, of delicate and feeble frame, particularly in *lean children* (italics supplied) there frequently exists in this (interscapular) situation a bronchophony very similar to the laryngophony, already noted." I was not able to detect the weakened inspiration at the apex, which Grancher²⁷ states is due to bronchial gland disease, and antedates the bronchophony, though faint breathing is commonly present in very early apical lesions. Bronchophony over the sternum was not observed.

Dilated veins over the anterior aspect of the thorax coexisted with vertebral bronchophony in 51 instances, and these cases gave 69 per cent. of positive reactions to tuberculin.

Some years ago Eustice Smith²⁸ called attention to the venous hum heard over the manubrium sterni, when the head is hyper-extended, which disappears as the head assumes its normal position. He considered it a valuable sign of bronchial gland tuberculosis, and attributed it to the pressure upon the left innominate vein by the glands at the lower end of the trachea. Inasmuch as it is uncommon after the thirteenth year, and as one-half of the 78 of our cases who presented this sign failed to react to tuberculin, its value can be seriously questioned. It seems to be especially common in short necked children.

RALES. A little over one year ago, Miller²⁹ and Woodruff drew attention to the presence of crepitant rales in the fourth, fifth, and sixth interspaces at about the mid-clavicular line in many of the children suspected of having tuberculosis. A positive diagnosis of tuberculosis was made in 82 of the cases presenting fine rales near the nipple. Miller and Woodruff considered the rales very suggestive of a tuberculous lesion at that region.

Rales were present in 46 of 137 of our cases, and except in a very few instances were located in the region of the mid-clavicular line in the fourth and fifth interspaces; 65 per cent. of children presenting rales reacted to tuberculin, and 38 per cent. of children in whom rales were not detected reacted. Rales were present in 46 per cent. of children reacting to tuberculin, and in 22 per cent. of those who did not react.

As only one examination was made in over half of the cases, the observation has less value, as the rales may be heard at one

²⁶ Camac, op. cit., p. 178.

²⁷ Bull. acad. de méd., 1906, lxx, No. 36. Abstract, Jour. Amer. Med. Assoc., 1906, xlvii, 2041.

²⁸ Wasting Diseases of Childhood, London, 1899, p. 309.

²⁹ Jour. Amer. Med. Assoc., 1909, lii, 1016.

examination, and not at another. They seem to be as common in the robust as in the frail child. These rules may indicate a tuberculous focus at that point; but the fact that it does not tend to spread, and later give definite signs of tuberculous infiltration, nor leave postmortem evidence of a primary disease at that point, is against this supposition.³⁰

RADIOGRAPHY. The x-rays are very valuable in the diagnosis of enlarged glands. Their use requires, however, perfect technique and a large experience in this particular line of work before they are of value. De la Camp considers it the most difficult of x-ray work.

Through the courtesy of Dr. Arthur C. Heublein, I have been able to compare the physical signs with the x-ray plate in 50 cases. Calcified glands are recognized by their sharp, clear-cut shadow. Cheesy glands, according to Nagel, give a shadow of less density, and with less clearly marked boundaries. The earliest evidence of tuberculosis of the bronchial glands seems to be a shadow that extends from about the anterior tip of the third rib on the right upward to the first rib. This shadow extends to the right of the vertebræ for a variable distance. It "bulges," as it were, into the region normally occupied by the inner aspect of the right lung (Figs. 2, 3, 4, 5, 6). In Fig. 2 the glands can be seen extending well up to the apex. Since making this observation, I find that Sluka³¹ has arrived at identically the same conclusion. In very young infants he found that the lung adjacent to the glands was practically always involved. He states that the pulmonary lesion may heal so thoroughly that no pathological lesion can be found at autopsy, though the lesion in the glands persists. Krämer attributes this "eaten out" appearance, sometimes observed at the border of the shadow, to the engorgement of lymph and bloodvessels. Swollen, but not cheesy glands, Nagel states, are less clearly or not at all recognizable.

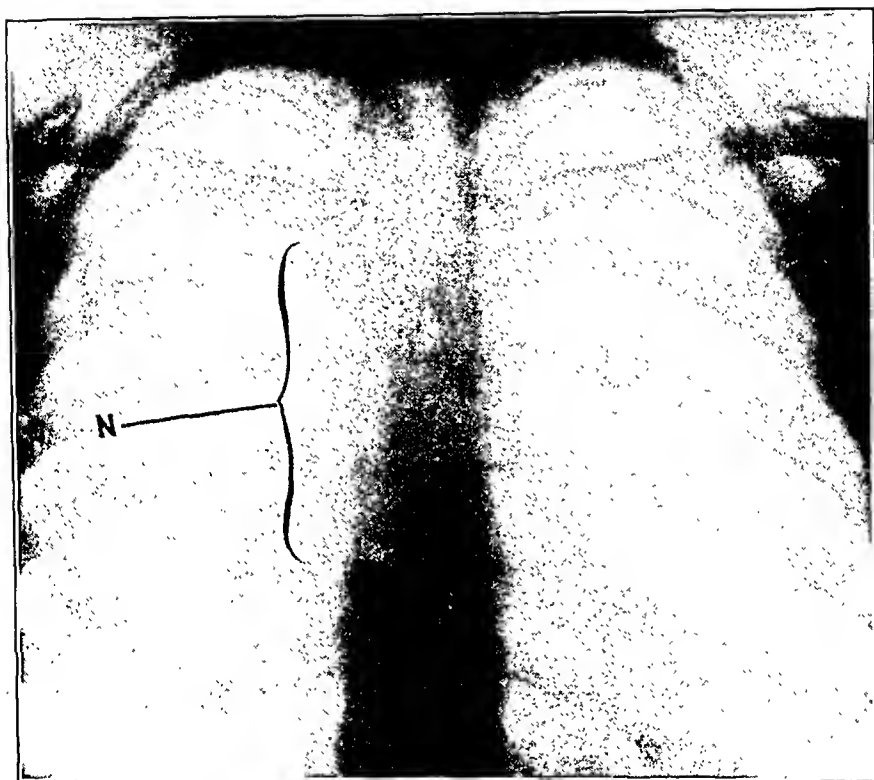
Recently I had an opportunity apparently to confirm this. A patient presenting a large mass of cervical glands, entered the Hartford Hospital for operation. A gland fully an inch in diameter, situated nearly behind the left clavicle, failed to cast a shadow, though the bronchial glands could be distinctly seen. At the operation it was found that the gland behind the clavicle was not caseous. It is possible that the dense muscles in which the gland was imbedded, obscured its shadow. A chain of glands can often be seen along the right border of the heart. The glands about the trachea give more diffused shadow than the hilum glands.

Dr. Heublein obtained the best results when the anterior aspects of the chest was in contact with the plate. The large infratracheal

³⁰ In the discussion of this paper Dr. John H. Lowman said that he attributed these rules to the congestion of the lymph vessels from the presence of the enlarged bronchial glands.

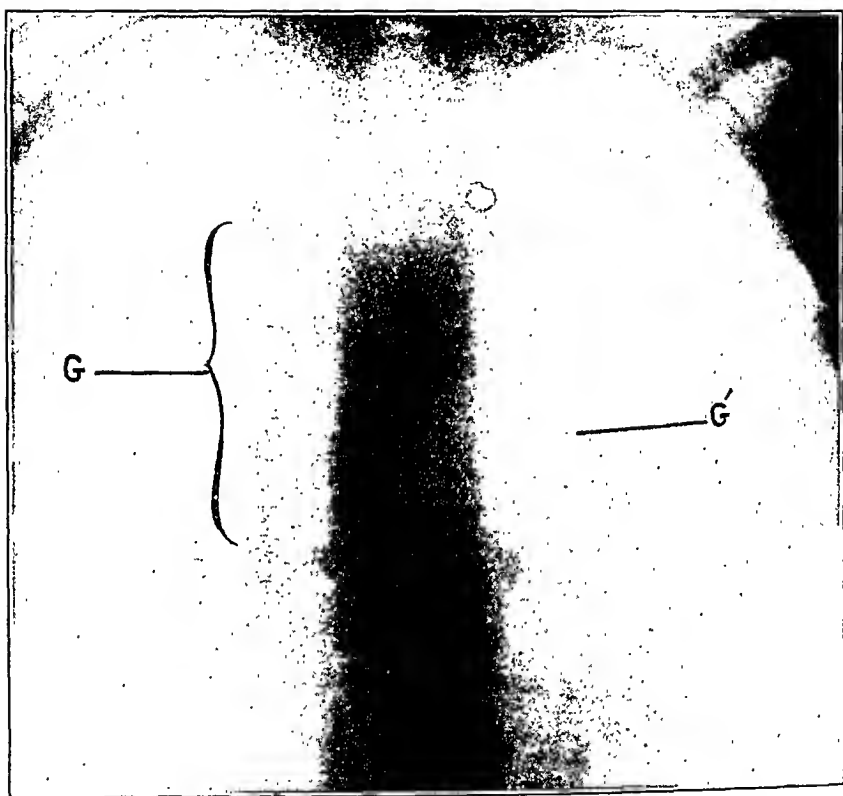
³¹ *Wien. klin. Woch.*, 1910, xxiii, 156.

FIG 1



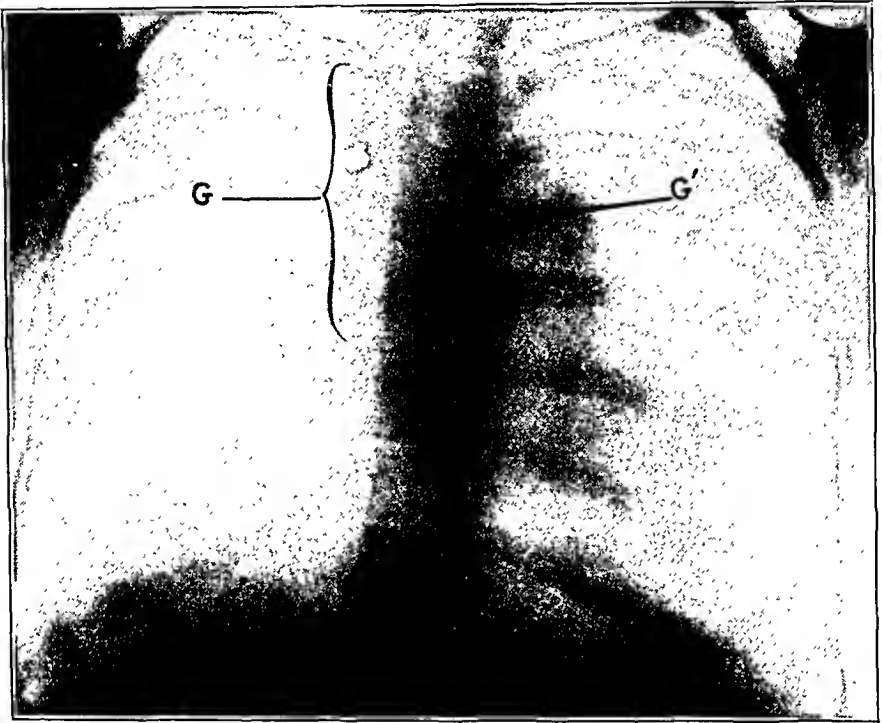
This child, aged twelve years, had none of the signs of bronchial gland enlargement, and was twice negative to the tuberculin skin test. The normal contour of the root of the right lung is shown at N. Compare this with the shadow of the bronchial glands in the succeeding pictures. In this case, as in all the others, the physical signs were recorded before the x-ray picture was taken.

FIG. 2



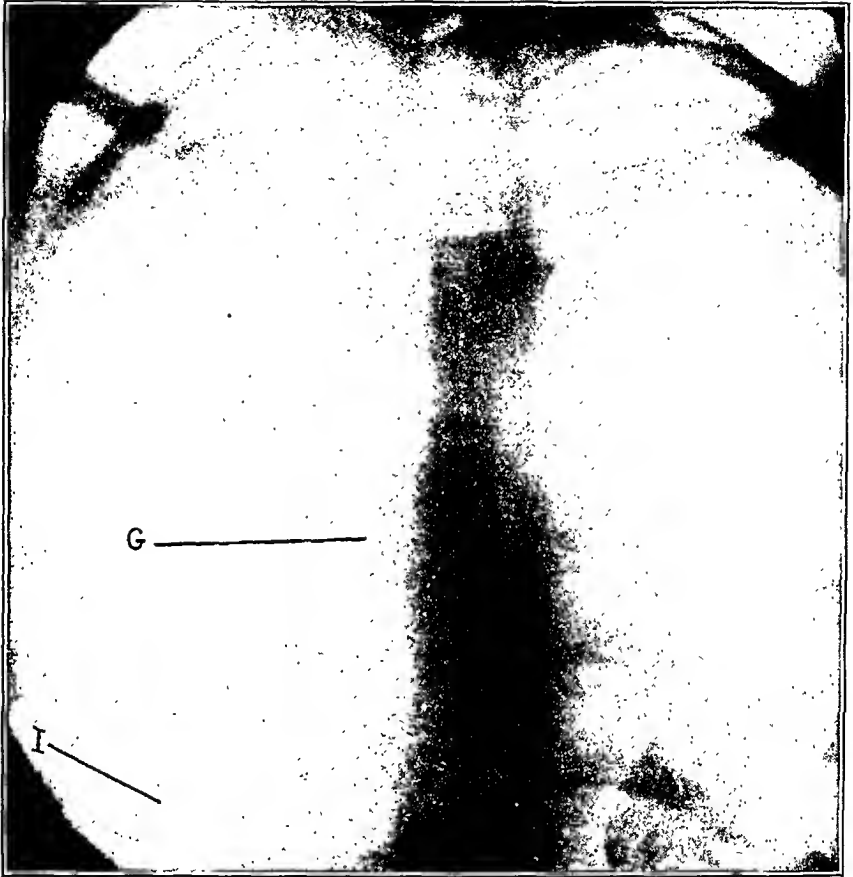
This child, aged seven years, had some retraction and diminished expansion at the right apex. Spinalgia was present over the upper thoracic vertebræ and the fifth thoracic spine was dull on percussion. There was no vertebral bronchophony. The tuberculin test was negative; repeated in six months with the same result.

FIG. 3



This child, aged eleven years, had some retraction below the right clavicle. Neither spinalgia nor vertebral dulness was present. Vertebral bronchophony was noted and the tuberculin test was positive. The glands extending upward along the right side of the trachea can be seen at G, and a gland above the left bronchus is indicated at G'.

FIG. 4



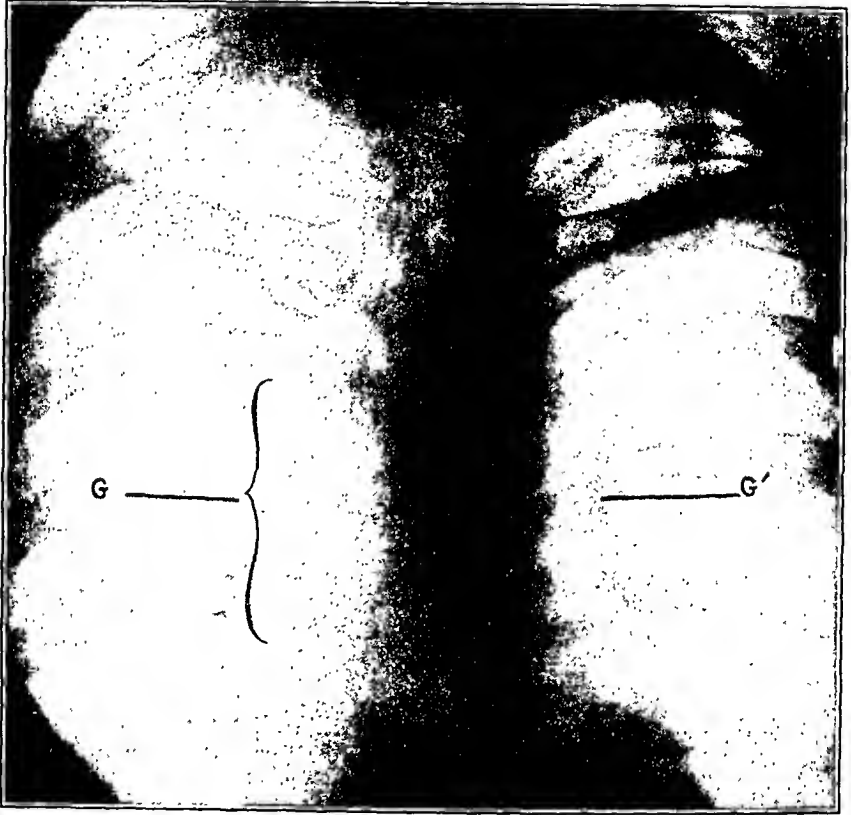
This patient, aged thirty-two years, showed slight lagging and muscle spasm at the left apex. Tenderness was present above and below the right clavicle and in the fifth right interspace in the parasternal line. Spinalgia was exquisite. There were both vertebral and paravertebral dulness (bilateral). Bronchophony over the vertebræ was present, but not marked. There was slight dulness at the apices, where a few fine rales were heard; rales also in fifth right space near the sternum. The x-ray plate showed deficient aëration at both apices and slight mottling at the right. An enlarged bronchial gland (presumably the infratracheal group) is indicated at G, while at I there is a small area of infiltration.

FIG. 5



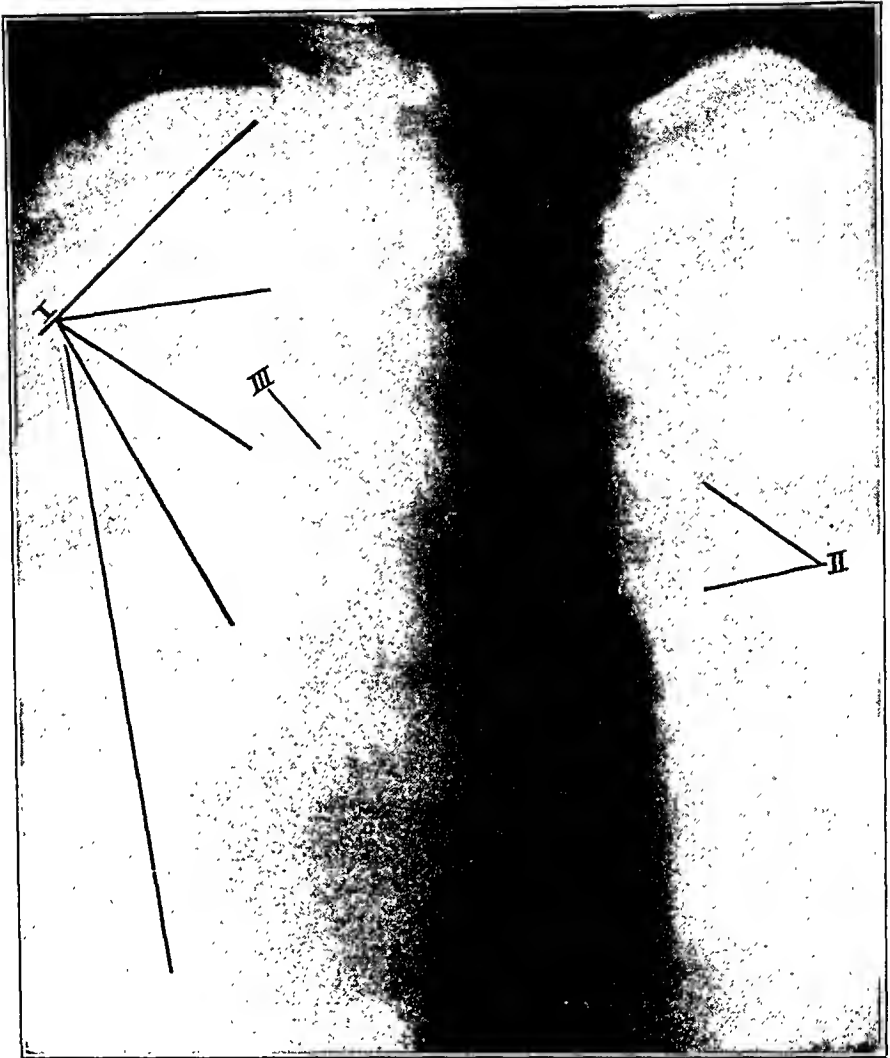
This patient, aged forty-nine years, had the usual signs of slight infiltration at the right apex. Vertebral and paravertebral dullness and vertebral bronchophony were present. Twice negative to the skin test and subsequently positive to the subcutaneous test. The patient has since died. The x-ray plate showed deficient aëration at the right apex and a large mediastinal tumor.

FIG. 6



In this patient, aged forty years, the signs were those of early infiltration at both apices and along the anterior borders of the lungs. Spinalgia was present, and there was slight dulness to the right of the fourth and fifth thoracic vertebræ. Vertebral bronchophony was present from the fifth to the eighth thoracic spines. It extended somewhat to the left. Individual tubercles can be seen above the right clavicle. The increase in thickening at the root of the lung, due to bronchial glands, is indicated by G, while a hilum gland can be seen at G'.

FIG. 7



Woman, aged forty-five years, with suspicious signs at the left apex and a positive tuberculin reaction. The apices are not shown in this picture, but in a subsequent one early infiltration at the left was apparent. Calcification of the costal cartilages is indicated by I; a small hilum gland at II, and extending upward from the gland at III, one sees streaks extending up to the left apex. These are probably thickened lymphatics, and indicate the path of infection from bronchial gland to the apex.

glands lie posterior to the heart and do not cast a shadow in most cases, though it is not uncommon to see small glands through the heart, near its periphery. Fig. 4, however, shows this infratracheal gland very distinctly opposite the second intercostal space on the right.

Quite commonly one sees an enlarged gland close to a bronchus, which is seen in cross sections. Fig. 7 seems to show the line of infection along the lymphatics from a hilum gland to the apex, which Sturtz³² has described. The enlarged glands can be readily seen with the fluoroscope, and their appearance has been described by Minor.³³ An x-ray plate, however, allows more careful study, and is a permanent record.

Inasmuch as tuberculosis is not the only disease that causes enlargement of the endothoracic glands, it is desirable to substantiate the diagnosis by the use of tuberculin. The skin test of von Pirquet is the one of choice in children, bearing in mind, however, that occasionally a reaction will be obtained from the subcutaneous test when the skin test is negative. The intensification of pressure symptoms following the subcutaneous injection is indicative of a focal reaction in the glands.

CONCLUSIONS. 1. Tuberculosis of the bronchial glands often exists as a distinct clinical entity, capable of diagnosis.

2. While the diagnosis is more readily made in children, it can frequently be made in adults.

3. The presence of dilated veins over the anterior aspect of the chest, spinalgia, interscapular or vertebral dullness, and vertebral bronchophony speak strongly for enlarged bronchial glands, the tuberculous nature of which is practically assured when in addition to the above the individual is under weight and has a paroxysmal cough and the symptoms of the tuberculous toxemia.

4. The recognition of the disease, while it is still limited to the bronchial glands, is of the utmost importance, as we know the most salutary results of tuberculin therapy are obtained in glandular tuberculosis.

³² Proc. Fourth Congress Tuberculosis Specialists, quoted by Wolff and Eisner. *Ophth. and Cutan., diag. of Tuberculosis*, London, 1908, p. 172.

³³ *New York Med. Jour.*, 1910, xci, 573.

PELLAGRA, WITH A REPORT OF TWO CASES WITH
NECROPSY.¹

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CLINICAL REPORT BY DR. ANDERSON. CASE I.—Mrs. D. E., white, aged twenty-two years. The family history is negative except for the fact that one brother died with pulmonary tuberculosis. The patient had the diseases common to childhood. Catamenia occurred at sixteen, and was regular, but has been absent since March, 1909. She has always been in good health until four years ago, when she began to have gastric disturbance. This began in the spring, but became less severe during the fall. The following year, in March, her gastric symptoms returned and she had a persistent diarrhoea, with several watery stools a day. Later, the dorsal aspect of her hands and wrists became reddened and the palms roughened. There was a reddened patch on the neck, at the root of the hair, and on the nose and at the corners of the mouth. The patient states concerning her hands: "They were red, itched, and were sore, and looked just like they had been dipped in hot water and scalded." The elbows were also red and roughened. The mouth and tongue were sore. Salivation was profuse. Hunger and thirst were excessive, and there was considerable loss of weight. She was able to do her housework, however, and was not confined to bed. After a short time the skin of the hands and of the patches on the nose and neck peeled off. The diarrhoea gradually grew better, and in the fall the patient gained flesh and seemed to be in fairly good health. In March of the following year the eruption again appeared as before, accompanied by the symptoms previously enumerated, but they were more severe, especially the diarrhoea, and the patient became so ill that she was confined to her bed. In August, 1909, she was taken to a general hospital, where she remained for a month. When she left the hospital she was better; the skin of her hands had again peeled, but the hands were roughened. She was unable to take up her housework, however, on account of weakness and nervousness. She also was not able to walk well, and at times felt dizzy and blind.

The patient became disturbed mentally in January, 1910, and was admitted to the Western North Carolina Hospital for the Insane February 27, 1910. The duration of the mental trouble

¹ Read at a meeting of the College of Physicians of Philadelphia, December 7, 1910.

before admission was one month. Prior to admission she was sleepless, restless, apprehensive of bodily harm when left alone, silly in speech and behavior, and had hallucinations of sight. At one time she threatened suicide. The physician who committed the patient made a diagnosis of "neurasthenia bordering on melancholia." (This diagnosis has frequently been made in cases which later proved to be pellagra.)

Since the patient has been in the hospital she has been emotionally unstable, weeping without the slightest cause, and occasionally smiling in a wan way. As a rule, however, she has an anxious, apprehensive expression on her face. She says that her blood and nerves are wrong; that her uterus and stomach are terribly diseased. She complains of excessive pains in her ankles and knees. She says, also, that her back is weak and causes her pain. There is marked salivation—in fact, so great is this that her pillow is frequently wet by it. Her appetite is ravenous and her thirst is excessive. Her mouth and tongue are sore and she complains of a burning sensation in the œsophagus and stomach. She is constantly complaining of these symptoms and begs the doctor to give her medicine for them, as long as he is in sight. She also begs him pitifully not to let her die. In answering questions she is more or less confused, at times, and her memory is defective. She speaks in a monotonous voice, never varying the tone. She walks with difficulty, but for a few days after admission she was able to walk from her ward to the porch without assistance.

Physical Examination, March 19, 1910: The patient (Fig. 1) is well developed, but very much emaciated. She has an anxious, agitated expression on her face and cries and moans almost constantly, bewailing her fate. At times she has a mask-like expression of the face. There are no asymmetries of face. The ears are well formed; lobules attached. The pupils are regular; contracted; react sluggishly to light and to accommodation. There is no nystagmus and no strabismus. The conjunctivæ are sensitive to touch. The tongue is protruded straight, but marked coarse tremors are present. The edges of the tongue are reddened and the central part is covered with a brownish coating. Salivation is present to a marked degree. There is a reddish-brown discoloration extending from the base of the neck upward to the hair-line, and there is also a reddish purplish discoloration on the dorsal aspect of the hands, extending an inch or two above the wrist (Figs. 2 and 3). This is symmetrical on each side. Nothing abnormal is noticed about the palms. The normal lines of the skin on the dorsal aspect of the hands seem to be lacking. The chest is symmetrical, more or less flattened, and the subclavicular fossæ show a more or less marked depression on each side. No abnormality can be determined by percussion, but auscultation reveals harsh breath sounds at the left apex. The heart is apparently normal in size and no murmurs can be heard. The



FIG. 1.—Photograph of the patient (Case I), showing the retraction of the head.

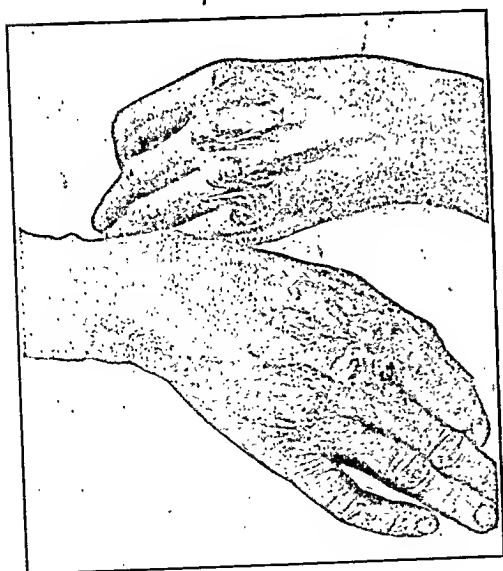


FIG. 2.—Photograph of the hands, showing the pellagrous eczema on the dorsal surfaces

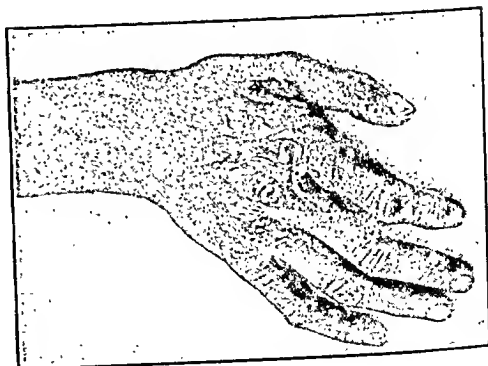


FIG. 3.—Photograph of the right hand alone, showing the eczema more distinctly.

abdomen is slightly distended. No masses can be felt. The abdominal organs are apparently normal. The liver is contracted. It extends from the fourth interspace to the seventh rib in the mid-axillary line. The abdominal reflexes are absent. The plantar reflexes are greatly exaggerated. The Babinski reflex and ankle clonus are not obtained. The patellar reflex is greatly exaggerated. The patient complains of excessive pain when she is tested for ankle clonus. There is a marked, coarse tremor of the head, and movements of the hands and arms are more or less athetoid or ataxic. There is marked incoördination in the upper extremities, the patient being unable to place her hand on her nose with the eyes shut. The station is poor; the patient shows a tendency to sway and would doubtless fall if she were not caught when the eyes are closed. The gait is more or less spastic and uncertain. She cannot walk without assistance, and walks with the feet spread wide apart. Apparently she has difficulty in recognizing the difference in the heat and cold tests on the feet and legs, but she could tell the difference when the tests were applied to her abdomen. The test for touch and pain could not be carried out on account of the patient's failure to co-operate. There are many coarse tremors of the hands when they are extended.

Smell: Turpentine; castor oil; ammonia, not recognized; camphor, correct.

Taste: Sour, correct; salt, correct; bitter, sour; sweet, not recognized.

March 30, 1910. Numerous bullæ have developed on the dorsal aspect of patient's hands, and in places these have broken, leaving sores. There is a marked reddening all over the dorsal aspect of the hands. There is also marked scaliness with excessive redness of the forehead, on the nose, and on the back of the neck. The elbows are very much roughened. The patient is quite emotionally unstable. She is fearful that she will die, and cries a great deal of the time. She almost invariably has an anxious, set expression on her face, and although, at times, she laughs in a silly way, her expression is more or less fixed all the time. There is marked redness of the mucous membrane of the mouth; the tongue is reddened and fissured, and there is an ulcer at each corner of the mouth. There is also marked salivation. She walks with difficulty—in fact, she cannot walk alone at all. The patellar reflex is greatly exaggerated. She eats ravenously and is excessively thirsty. She also, at times, has slight opisthotonos, and complains of excessive pains in her legs. She also states that her hands burn terribly. Her bowels are constipated. She sleeps scarcely at all.

April 15, 1910. The patient is growing much weaker. She has a persistent diarrhœa, with several watery, foul-smelling stools a day. She is excessively nervous and her muscles twitch a great deal. This condition exists even in her sleep. She is greatly depressed

and is apprehensive that something terrible is going to happen to her. She cries a great deal and begs constantly for food and water. The deep reflexes are still greatly exaggerated. The opisthotonos is increasing in severity. She cannot walk at all and has to be carried to her chair on the porch.

May 1, 1910. The patient is confined to bed. There are marked clonic convulsive movements of her legs and arms, and twitchings of her whole body; in fact, she is scarcely still a minute. The slightest touch produces a marked convulsive movement. She is still excessively thirsty and eats ravenously. She has a persistent diarrhœa, with numerous watery, foul-smelling stools each day. The dorsal aspect of her hands presents a reddish, purplish appearance. The epidermis is coming away in scales. There is also a scaliness about the corners of the mouth, on her nose and forehead, on the back of her neck, and on her elbows.

May 8, 1910. The patient is much weaker. Speech is thick and she expresses herself with difficulty. At times she is delirious. There is a very marked opisthotonos and there are clonic convulsive movements of the arms and legs. At times there are tonic spasms, and marked muscular twitchings are present most of the time. The mouth is excessively reddened, with saliva drooling from it, and the tongue is beefy in appearance. The deep reflexes are still greatly exaggerated, but are not so much exaggerated as they were for a time.

May 9, 1910. The patient died today.

March 1, 1910. Urinalysis: Straw-colored, flocculent precipitate; slightly acid; 1010; trace of albumin; no sugar; no casts; many urates; a few epithelial cells.

March 3, 1910. Examination of sputum for tubercle bacilli, positive.

April 23, 1910. Urinalysis: Light amber; clear; acid; 1013; no albumin; no sugar; no casts; many epithelial cells.

April 23, 1910. Feces examined—no hookworm ova found.

CASE II.—E. A. H. (under the care of Dr. Jas. K. Hall. Notes by Dr. Hall).

This man was admitted to the Western North Carolina Insane Asylum in 1888, at the age of forty, from a county in the extreme western portion of the State. He had been married for ten years and had a wife and two children. He was a gunsmith and cabinet-maker, but he had no education and was without property. For ten years or more before admission he had been wandering about over the neighborhood, had done little work, and for perhaps more than ten years he had been looked upon as mentally abnormal. At times he was mute for days; sometimes he was extremely irritable, had visual hallucinations, and he occasionally threatened violence to members of his family and his neighbors. He attempted suicide, and pending admission to the hospital he was kept in the county jail for several weeks.

When admitted to the hospital the patient was a quiet dement, in rather frail physical health. Two years after admission he had a severe attack of influenza, but he made a good recovery, and six years later he had measles. When able, he worked on the farm, but there was a loud, systolic murmur, and at times the feet became so swollen that confinement to bed was necessary for a short time. In the latter part of 1903 he was transferred from the main building of the hospital to the colony, where the patients all engage in outdoor work, and this man found employment in breaking stones with a hammer, for macadamizing the roads. The note was made that his physical health during the winter of 1903-04 was first-rate, but a line in his history, dated April 1, 1904, states that he has an eczema-like eruption on his hands, and for that reason he is left indoors. On June 16, 1904, it was noted that he had been in bed for several days because of disturbances of cardiac compensation; that he had been unusually depressed and ate little, but the condition of the hands had improved. In the early part of October he was said to be very weak, emaciated, and there were bedsores. The physical condition had improved by the spring of 1905, and he was again able to be out of bed. For the following two years he remained in the hospital building, doing a little work in the ward, and it is presumed that his physical health was fairly good, inasmuch as no mention is made of illness in the history. On May 15, 1907, the following note was made: "This patient was transferred from the hospital building to the colony about April 1; he busies himself in helping to keep one of the buildings in order, but he is profoundly demented, and the scope of his intellectual activity is extremely circumscribed. It is impossible to induce him to raise his voice and he speaks always in a whisper. His general health is not robust, but apparently fairly good." The old man remained at this colony until September 24, 1909, when he was again placed in a hospital ward because of failing physical health. At that time the backs of the hands looked as if they had been badly sunburned. The bowels were loose, the appetite was failing, and he was losing in weight. The gait was uncertain and tottering; the movements of the upper extremities were athetoid; the protruded tongue was tremulous, and the deep reflexes were exaggerated. Ankle clonus and Babinski's sign were absent. No doubt was felt that the condition was due to pellagra.

The decline was steady and progressive. The diet was restricted principally to milk, and although sufficient nourishment was taken, emaciation increased. Dementia was so far advanced that no intelligent statements could be elicited from the patient. Diarrhœa was troublesome, and all control of the movements was soon lost. Tonics were given and efforts were made to control the diarrhœa, but without avail. As the emaciation increased, bedsores developed. The bed was soiled every few minutes. The bowel

movements were a dark, grayish liquid, and peculiarly offensive. The lower extremities became drawn, and efforts to extend them seemed to cause great pain. There were almost constant, apparently purposeless, movements of the upper extremities, extremely awkward and incoördinate. He was extremely restless and his behavior induced the belief that he was annoyed by visual hallucinations. As the disease progressed, the muscular disturbance became more marked. In addition to the gross movements of the upper extremities, there were spasmodic movements of the fingers. The eyelids frequently moved rapidly. At times there were clonic, convulsive-like movements of the whole body, of momentary duration. Not infrequently an unusually loud inspiratory grunt could be heard, due probably to spasmodic contraction of the diaphragm and other inspiratory muscles. Firm pressure on the skin seemed not to produce pain, but the gentlest tap on any part of the surface caused generalized, clonic muscular spasm. Pupillary abnormality was not noted. The temperature was never much above normal and in the last days it was slightly subnormal. The pulse became quite small and rapid. Urinalysis showed a trace of albumin and a few hyaline casts. Repeated differential blood counts invariably showed an increase in the number of large lymphocytes. One count gave the following result: Polymorphonuclear neutrophils, 52.75 per cent.; eosinophils, 2.5 per cent.; large lymphocytes, 22.75 per cent.; small lymphocytes, 22 per cent.

Death occurred January 3, 1910.

The necropsy showed nothing unusual. Emaciation was extreme; the muscles were quite red; the lungs and pleuræ were normal; the heart was somewhat enlarged, and the mitral leaflets were gnarled. The spleen was small, dark, and tough; the liver was about normal in size and consistence, and the intestinal wall was thin and pale. The kidneys were small; the capsule was adherent; the organs were tough and the cortex shrunken.

Remarks. It will be observed that this man was an inmate of the institution for twenty-two years before his death. During this time he had lived a sheltered, protected life, in a climate noted for its healthfulness. He was probably the first patient in the hospital to develop pellagra. It is scarcely to be doubted that the soreness of the backs of his hands noted in 1904 was the dermatitis of pellagra. For the following five years there were apparently no symptoms of the disease. The final attack developed late in the summer. For more than two years before his last illness he lived in a colony with seventy-five other patients, almost a mile from the hospital, and during this time he was not near any pellagrous patients. His diet and his hygienic conditions were exactly those of a thousand other patients. Contagion was not possible. If the food and surrounding conditions caused the disease it seems strange that he alone should have been affected.

THE PATHOLOGY OF PELLAGRA BY DR. SPILLER. The number of clinical cases of pellagra reported in this country has become quite large since the disease was first recognized here a few years ago. So far as I know, no report of a necropsy in any of these cases has been published, and it is important to determine whether the pathology of the American cases conforms to that of the European or not. It is presumable, however, as the symptoms of the disease are essentially the same in our country and in foreign lands, that the pathology will not vary greatly. Pathological reports are found chiefly in the Italian language, and the only one in English known to me is by Batten, who studied the spinal cord in three cases described by Sandwich.² Batten found degeneration of the posterior columns in two cases, but the third case showed practically no change. He believed the sclerosis of the posterior columns to be of root origin. The process was a chronic one, as shown by the fact that the posterior columns were extensively sclerosed and no degeneration was revealed by the Marchi stain. This report by Batten is especially interesting in that it seems to show that the degeneration in the spinal cord was not rapidly progressive, otherwise changes would have been detected by the Marchi stain.

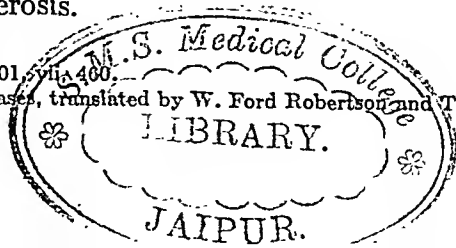
Tanzi,³ in the recent English translation of his text-book, says that Tonnini, in 1883-1884, was the first to associate the spinal phenomena of pellagra with primary spinal lesions (cellular pigmentation) of the anterior and posterior horns of the spinal cord. In cases of long standing there may be general or local œdema of the brain, hyperemia, and thickening of the meninges, chronic internal hydrocephalus, and sometimes softening of the cerebral substance and hemorrhages. Accumulations of pigment are also to be observed in the cells of the spinal cord and in those of the sympathetic ganglia. The spinal cord at an early stage exhibits traces of systemic degeneration of combined type, that is, lesions of the posterior columns and of the crossed pyramidal tracts, as has been shown by Tuczak and Belmondo. There is also very often small-cell infiltration of the spinal meninges. In the acute cases the nerve cells of the cerebral cortex are swollen; in some instances the nucleus is displaced to the periphery, the processes are atrophic, and there is central chromatolysis.

Babés and Sion,⁴ in their monograph on pellagra, state that in most cases of this disease nothing peculiar was found in the spinal roots, but in other cases notable degenerative changes were found in the posterior roots. In the spinal cord were pronounced pigmentation of the nerve cells of the anterior and posterior horns, and often combined sclerosis.

² Jour. of Path. and Bact., 1901, vol. 4, p. 400.

³ A Text-book of Mental Diseases, translated by W. Ford Robertson and T. C. Mackenzie, Rebman Co., New York.

⁴ Nothnagel's System,



Babés and Sion, in their own cases, found the posterior roots often degenerated, and the degeneration of the posterior columns was secondary to this, but differed from that of tabes in the less involvement of Lissauer's zone and of the anterior root zone, unless the pellagrous changes in the posterior columns were far advanced, when these zones also were degenerated. The cells of Clarke's column were always affected. The cells of the anterior horns were degenerated, as were also the cells of the cerebral cortex. They regard the changes as produced by some poison.

Lukács and Fabinyi,⁵ in a recent paper, state that system degeneration of the spinal cord is rare in pellagra. The cerebral meninges in their cases were intact, but in one case the spinal pia was a little thickened in places and infiltrated with cells. They found no unusual arteriosclerosis, although Marianis records arteriosclerosis as constant in pellagra. The medullated fibers of the brain, cerebellum, and medulla oblongata were normal (Marchi's method, however, was not used). In two cases the spinal tracts were intact, in a third the columns of Goll were degenerated from the pyramidal decussation to the upper thoracic cord. Many cells of the posterior horns were degenerated from the cervical swelling downward, but less intensely in lower levels, and this cellular degeneration is supposed by the writers to have been the cause of the degeneration of the columns of Goll. Degeneration of these columns, they state, is very common in pellagra, and differs from that of tabes in that it is seen only in the cervical region, and in that Lissauer's zone is intact. The cells of Clarke's column were greatly degenerated. Nuclei of sensory nerves in the medulla oblongata and pons were scarcely altered, while motor nuclei here were intensely affected. The cells of the anterior horns were greatly degenerated, especially in the cervical region, and showed granular chromophilic elements at the periphery, and a homogeneous centre, with absence of nucleus. The cells of the brain cortex were likewise affected, and especially those in the central convolutions. The lesions, they state, correspond to those of ergotin, mercury, or aconite poisoning, and pellagra is a disease of toxic nature.

Parhon and Papinian⁶ seem to be the only investigators who have studied the neurofibrils in pellagra. They found the alterations less intense in the small cortical cells of the brain, and most intense in the Betz cells. The neurofibrils stained less deeply, were thinner, even fragmented. In some small pyramid cells they were not altered. In the large cells the neurofibrils were almost completely absent; in some they were preserved at the periphery and in the cell processes. Alterations were more intense in the cervical region than in the lumbo-sacral region, and were of the same kind as in the Betz cells.

⁵ Allg. Zeitsch. f. Psych., 1908, lxx, 657.

⁶ Comptes-rend. de la Soc. de biologie, 1905, lviii, 360.

Pathological Report of Case I (Case of Dr. Anderson). The nerve cells of the anterior horns of the lumbar region are intensely degenerated. The cell body is swollen, the nucleus is displaced to the periphery, the dendritic processes of many cells have disappeared, and the cell body shows intense chromatolysis, sometimes implicating the whole cell, sometimes leaving a zone of chromophilic elements at the periphery of the cell body. The cells of the anterior horns stained by the Bielschowsky silver stain show an absence or a fragmentation of the neurofibrils. There is no round-cell infiltration of the pia. The anterior and posterior roots appear to be

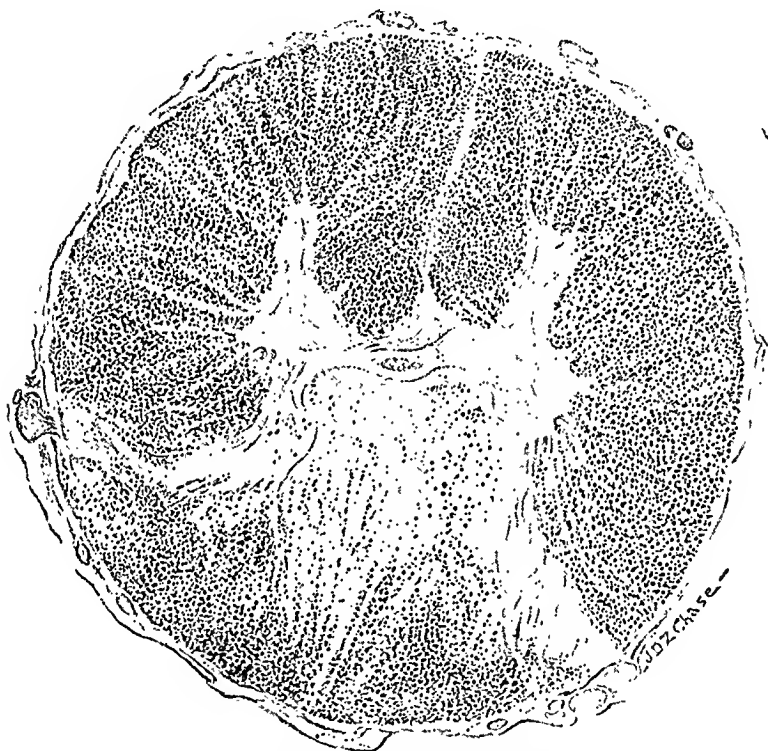


FIG. 4.—Drawing of a section of the thoracic cord from Case I, showing the diffuse degeneration of the posterior and lateral columns by the Marchi stain.

normal. Marchi's stain reveals diffuse degeneration in the posterior and antero-lateral columns, but less in the posterior columns near the gray matter. Numerous holes, from which nerve fibers have disappeared, are found in the antero-lateral columns. The pia is not thickened and the bloodvessels are not sclerotic. The thoracic cord is much distorted, probably as a result of injury at the necropsy. Here and there a swollen axis cylinder may be found in the antero-lateral columns. The cells of the anterior horns present the same condition as do those in the lumbar region. The cells of the columns of Clarke show similar changes. The degeneration of the posterior and antero-lateral columns by the Marchi

stain is pronounced (Fig. 4). Only the lowest part of the cervical cord was obtained. The anterior horn cells are in the same condition as are those in the lumbar region. The anterior and posterior roots of the eighth cervical and first thoracic segments, cut separately from the cord, appear to be normal. The capsules of the cells of the lumbar posterior ganglia show much proliferation of their lining cells, and the nerve cells are in part degenerated. Cells of the hypoglossus nucleus present a condition similar to that of the cells in the anterior horns, but of less intensity. The cells of Betz and the nerve cells of the deeper cortical layers in the paracentral lobules show changes similar to those of the anterior horn cells, that is, swelling, chromatolysis, and displacement of the nucleus (Fig. 5).

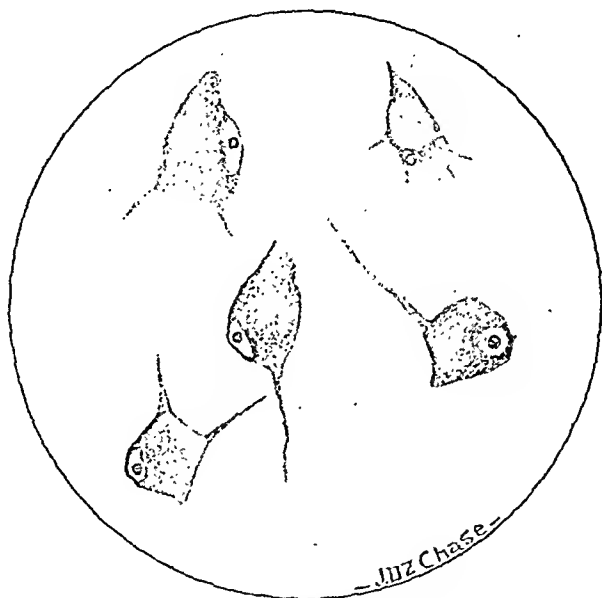


FIG. 5.—Drawing of nerve cells from the paracentral lobule and the anterior horns of the lumbar region. Cell of Betz from the paracentral lobule. One of the larger pyramidal cells of the deeper layers of the paracentral lobule. Cells of the anterior horn of the lumbar region. All these cells are much degenerated.

Pathological Report of Case II (Case of Dr. Hall). Only a small piece of the spinal cord was obtained, and this was from the thoracic region. The pia is distinctly thickened. Diffuse but slight proliferation is found in the lateral and posterior columns; the cells of the columns of Clarke are much swollen; the nucleus is eccentric; and the dendritic processes of some of the cells have been lost. The cells of the anterior horns are in a similar condition, but in some of these the chromophilic elements have disappeared from the periphery of the cell and are found nearer the nucleus; in others they persist only at the periphery. Spaces are found in the antero-lateral columns from which nerve fibers have disappeared. The vessels of the cord are somewhat sclerotic. The Marchi stain shows

intense recent degeneration in the peripheral parts of the posterior columns, in the crossed pyramidal tracts and anterolateral columns, but less degeneration directly in front of the crossed pyramidal tracts and in the median and ventral portions of the posterior columns. The connective tissue of the sciatic nerve and the intima of the vessels in the nerve are proliferated. The nerve fibers of this nerve are normal.

It is evident from the brief abstracts of the foreign representative papers treating of the pathology of pellagra that there is a difference of opinion as regards the systemic or non-systemic appearance of the degeneration in the spinal cord. This is a matter of some importance, as a toxic degeneration is more likely to be non-systemic. In the two cases I have studied the degeneration was diffuse. Indeed, from my own experience I have come to believe that, with the exception of Friedreich's ataxia, there are few disorders causing a truly combined systemic disease of the spinal cord. The degeneration observed in anemia is not systemic, but in the cases I have studied (quite a large number), it has invariably been a diffuse process. It is more intense than that I have observed in pellagra, but not of an essentially different character. The nerve cells, however, are much more affected in pellagra than in anemia.

Writers seem to agree as to the pronounced degenerative changes in the cells of the anterior horns of the spinal cord and of the cortex of the cerebral hemispheres in pellagra. It appears from the first case reported in our paper that the moderate degeneration of the pyramidal tracts predominated clinically over the apparently more intense alteration of the cells of the anterior horns, so that exaggeration of patellar reflexes was present.

The view has been expressed (Long) that the thickening of bone about the intervertebral foramina, possibly more in the cervical region, may be a cause of the symptoms. Unfortunately, only the extreme lower part of the cord in the cervical region in Case I was obtained, but posterior and anterior roots from this region, cut separately, showed no distinct degeneration, even by the Marchi stain. Had these roots been implicated in the intervertebral thickening, degeneration would have been detected in them. I have found no indication of root degeneration in the thoracic or lumbosacral region, and the alteration of the posterior columns, at least below the eighth cervical segment, is clearly endogenous, as it is also in the piece of thoracic cord obtained in the second case.

I must conclude, so far as a study of these two cases permits, that pellagra does not always produce, if indeed it ever does produce, a truly systemic disease of the central nervous system; but that the degeneration is caused by some toxic or infectious substance affecting all parts of the cerebrospinal axis, producing cellular degeneration and diffuse degeneration of nerve fibers in the posterior and antero-

lateral columns. It is not difficult to explain the mental symptoms when cortical degeneration is so intense as may occur in pellagra, and as is seen in the brain I have studied; and the insanity of this disease seems to be of a toxic or infectious character.

The constant involuntary movements of the limbs described by Dr. Anderson, and present also in Dr. Hall's case, are suggestive of the similar movements in strychnine poisoning. In pellagra the degeneration of the cells of the anterior horns probably causing irritation in the muscles innervated by them, the impairment of cerebral inhibition produced by partial degeneration of the pyramidal tracts, and the incoördination produced by the partial degeneration of the posterior columns, the cerebellar tracts, and the cells of Clarke's columns, may all assist in causing involuntary and constant movement. It is sometimes forgotten that holding the hand still and extended is a very perfect form of movement, requiring the degree of tonicity in the flexors and extensors of the limb exactly sufficient to maintain this position.

The spinal pia was considerably thickened in the second case, which was of long duration, but the thickening of the pia was not observed in the first case.

THE INFLUENCE OF THE TRENDLENBURG POSITION ON THE QUANTITY OF URINE EXCRETED DURING ANESTHESIA.

BY J. WESLEY BOVÉE, M.D.,

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At the meeting of the American Gynecological Society in 1909, I presented a report of investigations made in my clinic in the Columbia Hospital for Women regarding the influence on renal activity from anesthesia by ether and by chloroform during surgical operations. I had not then thoroughly studied the variation due to the Trendelenburg position, but recorded my having been greatly impressed by it. Eight cases were therein noted as illustrative, and five cases had been especially studied. Having recently studied eight cases of ether anesthesia and eight of chloroform, I present herewith a report on those observations. I believe the results demonstrate that almost no urine is received in the bladder while the Trendelenburg position is being employed.

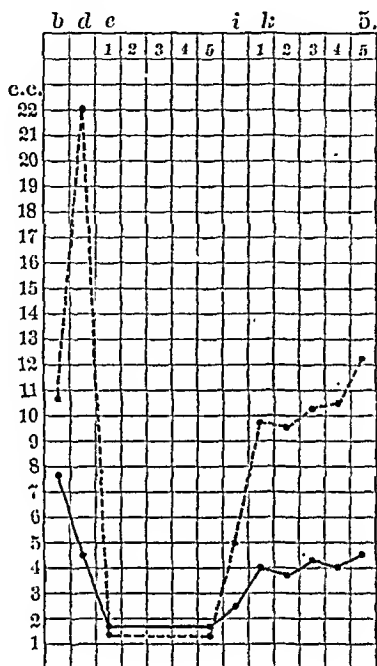
TECHNIQUE. The quantity of urine for a twenty-four-hour period fairly remote from the operation was obtained. Care was used to secure this knowledge without such influences as undue excitement, abnormal intake of fluids, or catharsis. The usual diet was continued until about twelve to fourteen hours before operation.

During this twelve to fourteen hours liquid food in very limited quantities was given. The bowels were moved two or three times, the last by an enema, and nothing but the one anesthetic given. No morphine, atropine, or other drug was used, nor was salt solution in any manner employed. The bladder was emptied by catheter when the administration of the anesthetic was begun; when about to place the patient in the Trendelenburg position, the clamp was removed from the permanent catheter and the bladder emptied. At the end of each fifteen minutes of the time the patient was in this position the bladder was drained. This was facilitated by the fingers pressing, intraperitoneally, upon the bladder. The urine was drawn immediately after the patient was returned to the horizontal position, and at the end of each subsequent fifteen minute period during the administration of the anesthetic, as well as when the anesthetic was stopped. The head nurse of the operating room, Miss Pugh, was very accurate and greatly interested in this feature of the work. During the following two days the urine was carefully measured, usually every fifteen minutes of the first two hours, by means of the permanent catheter.

<i>a</i>	<i>b</i>	<i>c</i>	<i>d</i>	<i>e</i>	<i>f</i>	<i>g</i>	<i>h</i>	<i>i</i>	<i>k</i>				
				1 2 3 4					1	2	3	4	5
1	660	35	20	0 0	35	1	10	4	10	10	8	8	8
2	870	41	2	0 0 0 0	64	4	0	4	4	4	4	4	4
3	600	45	16	0 0	38	12	7	4	7	2.5	2.5	2.5	2.5
4	630	32	4	0 0 0	48	6	23	1.6	1	1	1	1	4
5	26	22	0	19	4	15	1	1.6	2	2	2	8
6	1080	45	2	0	20	0	50	0	2	4	4	1	1
7	85	24	0 0	40	8	26	0	2	2	8	8	4
8	690	35	12	0	15	1	15	4	4	4	5	5	5
Ave.	7.9	...	4.45	1.9	...	2.3	4.0	3.7	4.3	4.0	4.5
1	840	38	44	0	23	8	30	2	40	40	40	40	40
2	1080	35	144	0	17	12	47	8	1.3	1.4	1.4	4	16
3	1110	41	4	0	29	0	24	7	6	6	6	6	5
4	840	35	32	1 0 0	50	0	16	0	0	0	0	0	0
5	480	40	20	10	8	42	12	8	12	20	24	24
6	1230	33	8	0 0	39	6	21	1	16	12	8	2	4
7	870	50	24	0	29	8	7	8	8	7	8	8	8
8	1800	36	168	0 0	31	0	9	0	0	0	0	0	0
Ave.	10.7	...	22.0	1.5	...	4.8	9.9	9.8	10.4	10.5	12.1

Explanation of the Table. The first series is ether anesthesia, and the second chloroform. The letter *a* signifies the case number; *b* the cubic centimeters of urine for twenty-four hours; *c* the number of minutes elapsed from the beginning of the administration of the anesthetic to the placing of the patient in the Trendelenburg position. The amount of urine excreted during that period is given in column *d*. The amount excreted during the employment of the Trendelenburg position is represented in fifteen minute periods under *e* 1, 2, 3, and 4; *f* records the exact number of minutes that position was used, while *g* represents the amount of urine drawn from the bladder when the patient's position was changed back to the hori-

zontal. The number of minutes the anesthetic was administered after using the Trendelenburg position is noted in column *h*, while the average amount excreted during each fifteen minutes of that period is found in column *i*; *k* 1, 2, 3, 4, and 5 represent urine quantities for the five periods of fifteen minutes each after the anesthetic was stopped. In every case the amount of urine became normal not later than twenty-four hours after operation.



The figures at the left of the chart indicate the quantity of urine for fifteen-minute periods, and the letters across the top of it refer to the corresponding columns in the table. The broken line represent the chloroform series, and the solid the ether series. It will be noted that in both series (ether 1.9 and chloroform 1.5) the current of urine in the Trendelenburg position suddenly comes down at the beginning to below 2 c.c. per fifteen minutes, and at once raises when the patient is taken out of that position.

In some of the cases in the table it will be noted that following the operation no urine was excreted during the hour and a quarter subsequent to the end of the operation. In each instance, at the end of twenty-four hours the quantity and quality were practically normal. In the chloroform series two patients excreted unusually large quantities during the early part of the anesthetic—one 144 c.c. in thirty-five minutes, and the other 168 c.c. in thirty-six minutes. These two cases extravagantly increase the average amount for fifteen minutes to 22 c.c., which is greatly in excess of the average (8.2) for the other six cases of the series. This gives a striking difference on the chart.

In the paper of 1909 I mentioned the marked lowering of the rate of urinary flow in the Trendelenburg position, estimating it at 32 per cent. In the series now submitted the decrease is for ether 58 per cent. and for chloroform 95 per cent. The decrease in the chloroform series is very much exaggerated, though in the six cases (omitting Cases II and VIII) of the series, in which the flow before using the Trendelenburg position was about normal, the decrease was 82 per cent. It might be said, therefore, that while the patient is in the Trendelenburg position the percentage of decrease in the excretion of urine is 58 per cent. in ether anesthesia and 82 per cent. in anesthesia by chloroform. That this great decrease is not, even in moderate degree, due to urine being retained in the renal pelvis is clear, for the rate of flow subsequent to changing the patient to the horizontal position is not suddenly greatly increased, being but slightly increased in the ether series, a little more in the chloroform series, and not for an hour and a quarter reaching a rate in excess of that of the period preceding the use of the Trendelenburg position. Nor can it be said that the bladder was not satisfactorily drained by the catheter, inasmuch as the fluctuations were always gradual and never sudden, except when changing to or from the Trendelenburg position.

If it can be concluded that the renal function is greatly lessened while the patient is in the Trendelenburg position, then the danger of that position is at once appreciated. In renal inefficiency, and cardiac and arterial lesions, it seems that the use of the Trendelenburg position introduces a special element of danger, and this less markedly when ether is used than when chloroform is employed as the anesthetic.

MULTIPLE ABSCESES OF THE NASAL SUBMUCOSA IN A CASE OF LEUKEMIA.

BY JOSEPH P. TUNIS, A.B., M.D.,

FELLOW OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA.

DURING April and May of 1909 I had the opportunity of examining, in the autopsy room of the Allgemeines Krankenhaus, in Vienna, the nares and accessory sinuses of ten adult heads in the clinical history of which leukemia had played an important part. In only one of these ten cases were multiple abscesses present. They gave the appearance of punctate hemorrhages over the entire nasal mucous membrane, more especially over the turbinate bones. This condition I believe is rarely met with, and therefore warrants detailed description. For permission to report these cases, as well as for the opportunity to study them, I am indebted to the courtesy

of Professor Hofrat Weichselbaum and Professor Stoerk. For additional notes on the clinical history I am indebted to Dr. Bartel. The history of this case is as follows:

Joseph G., a baker, aged forty-four years, married, was admitted to the General Hospital in Vienna on April 7, 1909, in the service of Professor Strumpell. The clinical diagnosis was diathesis hemorrhagica, with well-marked anemia, atrophy of the bone marrow, and lobular pneumonia. He died on April 16, that is, nine days later, and the autopsy was performed on the following day.

The patient's mother died at the age of seventy-six, from asthma and degenerative myocarditis. His father, at this time, was living and well. He had had no brothers or sisters. As a child he had scarlet fever and measles. At the age of fifteen he had a retropharyngeal abscess, and at the age of twenty-five a return of this abscess. At the age of twenty-one he had syphilis, and was treated in Professor Lang's clinic. At the age of thirty-five he married and has had no children. At the age of forty-three he had a severe attack of gastro-intestinal catarrh, with considerable colic. He states that at this time he vomited blood, and that his recovery was a tedious one. After an interval of several months there was a return of this gastro-intestinal trouble.

He had been a moderate drinker of alcoholic liquors. Since childhood he had often had slight hemorrhages from the oral mucous membrane, dyspnoea, and palpitation of the heart. His last illness began about three weeks before death with hemorrhages from the gums, epistaxis, and swelling of the cervical glands.

An examination of the blood on April 15 showed: (1) The red blood cells to be 1,368,000; hemoglobin, 20 to 25 per cent.; and the color index, 0.8 to 0.9, or a trifle less than normal. The rouleaux formation was diminished. There were no macrocytes, numerous microcytes, slight poikilocytosis, and a few faintly colored red cells. (2) Leukocytes, 3700; polymorphonuclear cells, 3 per cent.; lymphocytes, 45 per cent.; eosinophiles, 0.5 per cent.; Turck's irritation forms 2 per cent.; no mast cells. In addition, there were 29.5 per cent. of various cells, such as large mononuclear, marrow cells, and transitional forms.. (3) There were no blood platelets present; the coagulability was diminished.

The urine showed serum albumin absent; nucleo-albumin present; otherwise negative.

In the feces the chemical test for blood was positive.

Autopsy Notes. Acute lymphatic leukemia. Infiltration of the gums with gangrene of the upper jaw in the region of the incisors; leukemic infiltration of the nasal mucous membrane, with narrowing of the nasal cavity. Swelling of the lymphatic tissues in the pharynx, of the oesophageal and intestinal follicles, cervical lymphatic glands, and of the lymph glands in other regions of the body (the lymph glands are marrow-like, grayish white, and well circumscribed).

General anemia, acute splenic tumor, calcified tuberculous subpleural focus in the right lower lobe with adhesion to the costal pleura; oedema of the brain and of the lungs. Multiple punctiform hemorrhages in the mucous and serous membranes, as well as in the lymphatic tissues. Moderate arterio-sclerosis and atheroma of the aorta. Height, 175 cm.; brain weighs 1300 grams. The thymus is replaced by a large fatty mass. Patulous foramen ovale. Adipositas. Adenomas in the thyroid gland, to the right and above the middle lobe and not separated from it. Bone marrow (of femur) $\frac{3}{4}$ red. Grayish-yellow coagula in the bloodvessels. Chronic internal hydrocephalus with granulations on the ependyma. The body was muscular and apparently well nourished.

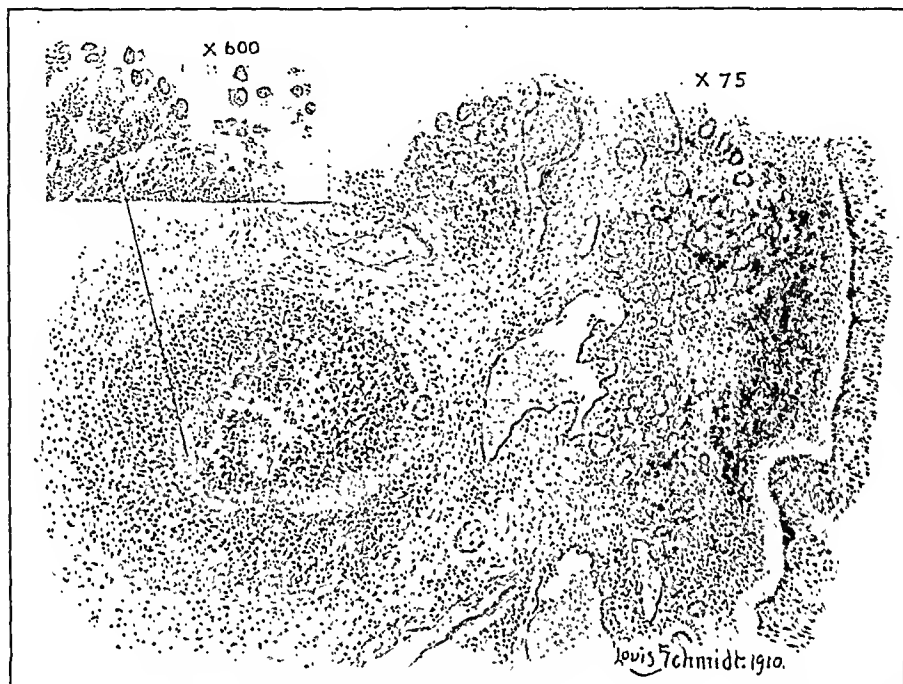
Upon opening the skull by the Ghon method a hemorrhage was seen in a very large sphenoidal sinus which measured 4.5 x 2.75 cm. Both the anterior and posterior walls of this sinus were extremely thin. On account of the numerous punctate hemorrhages over the entire nasal mucous membrane, more especially that covering the turbinates, I removed fragments from the middle and inferior turbinates for microscopic examination. Dr. Bartel also removed a number of fragments of tissues from almost every part of the body and subsequently confirmed the results of our examinations.

Microscopic Appearance. The affected mucous membrane is swollen to four or five times the ordinary thickness. The surface, in the sections examined, shows a decided desquamation and proliferation of the epithelium, which presents in places considerable irregular thickening and projection, while elsewhere the layer is thin, with loss of superficial cells. In the drawing (Fig. 1), proceeding from the right-hand side, there is, first, a layer of stratified columnar epithelium, beneath which a thin layer of oedematous tissue is succeeded by a superficial layer of round-cell infiltration. Adjacent to this there are a number of mucous glands and large injected vessels. To the left there is an abscess of the submucosa, with a loose, purulent centre; a border zone of the wall, showing in horseshoe form, largely made up of streptococci, to the outside of which is the inflammatory reaction zone of the wall.

In the section from which this drawing was made there were four of these abscesses present. It is a conservative estimate, therefore, to assume that there were at least one hundred similar abscesses in this man's nares.

Particularly in the thickened portion the epithelium is somewhat infiltrated with polymorphonuclear leukocytes. The tissue beneath the epithelium, down to the bone, is the seat of marked injection of the vessels, of focal hemorrhages, of a moderate diffuse oedema, together with a considerable mononuclear collection, especially near the surface, and a less marked diffuse polynuclear leukocytic infiltration. In the limits of the section four or five small abscess cavities occur, in the inner portion of the wall of each of

which are large masses of Gram positive streptococci. Scattered through the tissue small foci of similar organisms are occasionally met. Toward the surface of the membrane there are numerous phagocytic cells containing blood pigment granules, and in the looser portions of the structure, especially about the abscess, a fine fibrinous reticulum occurs. The mucous glands are of the usual distribution and number, frequently showing mucin in the interior.



Section through the mucosa and submucosa of a turbinate bone from a case of lymphatic leukemia showing hyperemia and inflammatory infiltration and a small suppurative focus, on the inner margin of the wall of which masses of streptococci are seen. These are shown at higher magnification in the upper left-hand corner, the reference line indicating the position in the larger field.

In the preparation examined it has been impossible to recognize, in the blood of the hemorrhagic foci or in that within the blood-vessels, features characteristic of leukemia. An especial round-cell infiltration, extending through the superficial portion, is probably rather inflammatory than of a lymphatic leukemic formation. The diagnosis of lymphatic leukemia in this case was made very positively from an examination of tissues elsewhere in the body. In another case, however, sections of the inferior turbinate showed undoubted evidence of a leukemic condition of the blood.

The history of a second case was as follows:

J. L., a coachman, aged twenty-eight years; died of pneumonia and leukemia. The mucous membrane of the turbinates was very much congested. I removed the posterior end of the left inferior

turbinate, sections of which, under the microscope, gave a clear picture of chronic inflammation. The bloodvessels were considerably enlarged and the lumen of the corpora cavernosa filled with leukemic blood.

Dr. James B. Herrick,¹ of Chicago, has reported a case of multiple abscesses of the brain in a case of leukemia. The patient was a young man, aged twenty-three years, who came under observation in March, 1905, and, despite the fact that the diagnosis was made promptly, he died in November of the same year. The abscesses were about the size of a ten cent piece in this case and were scattered everywhere throughout the cerebrum.

That interstitial hemorrhages are the rule rather than the exception in leukemia is a well-known fact, but that these hemorrhages, no matter how minute, may rapidly develop into abscesses is of considerable practical importance.

¹ Multiple Hirnhämorrhagien bei Leukämie, Festschrift, Dr. Hans Chiari, Wien, 1908, 317 to 333.

REVIEWS.

PREPARATORY AND AFTER-TREATMENT IN OPERATIVE CASES. By HERMAN A. HAUBOLD, M.D., Clinical Professor in Surgery in the New York University. Pp. 650; 429 illustrations. New York: D. Appleton & Co., 1910.

THE preface of this work sets forth convincingly the reason for its preparation and, unlike most prefaces, is not only logical, but readable. It emphasizes the fact—which is familiar to all surgeons—that the general practitioner is, as a rule, unfitted to make the arrangements for an important operation and to take care of the wound, and sometimes of the patient, during the critical stage of the after-treatment. That this is often not in the least the fault of the medical man, but is due to unavoidable lack of early technical training, or, even after such training, to the exacting demands of general practice, does not alter the situation. The result is that not only during, but often both before and after an operation, the regular medical attendant is to an extent displaced and supplanted, sometimes quite unintentionally and unavoidably belittled, not by the surgeon, but by his assistants and his special nurses, whose work during the preliminary and the after-treatment seems, by implication, to render the services of the medical man unnecessary or valueless. Partially as an outcome from this situation, and partially from motives that are as obvious as they are unworthy, has arisen the widespread and essentially dishonorable practice of giving the medical attendant a percentage of the surgical fee, a custom even more discreditable to a learned profession than is the “contingent fee” of our legal brethren.

The author says truthfully: “Much of this is due to the fact that neither the practitioner nor the patient have been properly educated in the matter. The practitioner has not devoted much energy to keeping in touch with modern methods of preparing patients for operation, and the patient has not been taught to understand that the work connected with or the services necessary in this regard is special work and demands a special fee.” He adds that it is even more true of the after-treatment of operative cases. “The surgeon does his operation, takes the fee, and the practitioner is compelled to carry out the after-treatment of the case at the usual rate of charge for a visit.”

It is a pity that so well written a preface should be marred by the next sentence in which the arrangement is said not to be "equable"—for "equitable"—and to stand in a causative relationship to the methods "of handling the financial end of the surgical proposition," an example, in spite of the undoubted truth of the assertion, of the use, or misuse, of several words that undoubtedly belong in the "Inferno" of our contemporary, "The Bookman."

The author continues, modestly, to say that if the book achieves nothing beyond placing the relationship of the practitioner and the surgeon to each other and of both toward the patient on a better basis, he will feel that a worthy object has been attained.

He has, however, achieved much more, and has written a book likely to be of great use not only to the general practitioner who is occasionally brought into close relation with a surgical case, but also to the young surgeon whose ideas require systematization, and even to the experienced surgeon about to take charge of an unusual case, or of an ordinary case under unusual circumstances.

Portions of the book particularly to be commended are those devoted to general considerations in non-urgent cases and to the preparation of the room, the bed, and the patient. The subject of diet in relation to operation is fully and adequately considered, although the author possibly over-emphasizes his objections to the "starvation" of patients a day or two before operation. If the expression is taken literally there is, however, no cause for cavil. The principles and details of feeding after operation are well summarized. The technique advised throughout the book is thorough, sensible, and dependable. Each surgeon is apt to have preferences in this respect, and, as might be expected, there is room for honest differences of opinion; but the methods here described, if intelligently employed, should, practically without exception, give satisfactory results.

The treatment of shock and of secondary hemorrhage, the dressing of the operative wound, the treatment of special symptoms, as thirst and pain, are thoroughly dealt with, and the special methods indicated in the preparation and in the after-treatment of particular operations, are fully and often minutely described. There is a useful chapter on artificial limbs. Another on anesthesia, general and local, would have perhaps added to the value of this excellent book, as, especially in emergencies, the medical attendant is so often the anesthetist. The illustrations are well chosen and well made. The book admirably covers its chosen ground and should be welcomed and widely read by the profession at large.

J. W. W.

THE PRESCRIBING OF SPECTACLES. By ARCHIBALD STANLEY PERCIVAL, M.A., M.B., B.C., Cantab., Senior Surgeon to the Northumberland and Durham Eye Infirmary. Pp. 159; 24 diagrams. Bristol: John Wright & Sons, Ltd.; London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd.; New York: William Wood & Co., 1910.

THIS book must have been written for those who are already acquainted with the subject; it is far too concise for the beginner, so that all it is likely to impart to the reader capable of understanding it are certain views and practices peculiar to the author, or perhaps to his country generally; thus, in the shadow test the concave mirror is preferred to the plane; two or three drops of a solution containing 8 grains of homatropine and 4 grains of cocaine to the ounce every quarter of an hour will paralyze the accommodation. In ordering glasses for hypermetropia, it is usually sufficient to deduct 1 D from the total hypermetropia if atropine, and 0.75 D if homatropine is used. The author would do away with the word presbyopia, under which term, if used at all, should be included hyperopia acquisita. The two-thirds rule is recommended in the correction of defective accommodation. He objects to Landolt's allowance of one-third of the absolute range of convergence.

The last chapter in the book gives the optical formulæ as applied to the constants of the eye, correcting lenses, size of images, etc., very interesting to the reader who is fairly well acquainted with elementary optics and understands the meaning of the formulæ and how they are derived; to others, among whom we fear is to be placed the great majority of students of ophthalmology, it is a closed chapter. Several tables are added in an appendix; one gives the squares of numbers from 10 to 100, another the values of the trigonometrical functions.

T. B. S.

A TREATISE ON DISEASES OF THE EYE. By JOHN ELMER WEEKS, M.D., Professor of Ophthalmology in the University and Bellevue Hospital Medical College (Medical Department of the New York University). Pp. 944; 528 engravings and 25 full-page plates in colors. New York and Philadelphia: Lea & Febiger, 1910.

THIS extensive work covers the entire field of ophthalmology. The style is singularly clear. Those parts which are usually difficult of comprehension, such as the development of the eye and certain parts of the anatomy, are so presented that even the beginner should have no difficulty in getting clear ideas. It is, moreover, thoroughly up to date. The microbic affections, as is to be expected

from its distinguished author, are especially well presented. Even the trachoma bodies are figured and described. We have failed to find any reference to the Wassermann reaction.

The removal of the clear lens in high myopia is stated to be now fully recognized in suitable cases, although it has not fulfilled the expectations of those who closely followed Fukala. While we are told that it should be employed only in carefully selected cases, how the selection is to be made is not clearly stated. The author advises, as a rule, that the total hyperopia should not be corrected except in cases of marked esophoria and strabismus. Early full correction of myopia is advocated. Before prescribing prisms for the correction of heterophoria, the advice is given to note the behavior of the eye under the correction of the ametropia, as the heterophoria, especially esophoria, may disappear when the error of refraction has been corrected. The necessity for a cycloplegic may be inferred from the text; it might be as well to make a direct statement to that effect. The most practical test for determining the refraction in intelligent patients is declared to be subjective examination with the trial lenses; the objective tests are valuable aids.

Among the newer subjects dealt with is arteriosclerosis. A short chapter is devoted to disease of the accessory sinuses as related to the eye.

The work is singularly free from slips of the pen and careless proofreading. Indeed, we have not come across a single instance of the latter. We do note, however, an inversion of words on page 122, where it is stated that in case of paralysis of the third nerve the *afferent* part of the reflex arc is interfered with, while the *efferent* part is intact.

The mechanical execution of the book leaves nothing to be desired. The type and paper are admirable. The numerous engravings are just what is needed to complete the descriptions. Most of the colored plates, of which there are 25, are unexceptional.

The work is to be recommended to everyone interested in the subject, from the undergraduate in medicine to the specialist in ophthalmology, for both of which classes the author tells us he has designed his work.

T. B. S.

THE PREVENTION AND TREATMENT OF ABORTION. By FREDERICK J. TAUSSIG, A.B., M.D., Lecturer in Gynecology in the Washington University; Obstetrician to the St. Louis Maternity Hospital, etc. Pp. 172; 59 illustrations. St. Louis: C. V. Mosby Co., 1910.

THERE can be no difference of opinion of the importance of the subject of which this little volume treats, since there is probably

no one condition more often met with by the general practitioner, few that give more concern to the conscientious man, and none which is treated more casually by a large number of the profession. The truth of all these statements will, we believe, be vouched for by all those doing work in the diseases of women. Certainly the casual attitude of the general profession has been painfully evident to all who do much consultation work along these lines. We therefore welcome any and all attempts to impress upon the profession their responsibilities in this direction. The author of this book claims no originality for anything except the manner of presentation. His experience has eminently fitted him for the preparation of the volume, and he has produced a very readable book, our only criticism being that the case histories might have been omitted without lessening the value of the work.

The book is well written and the deductions with regard to treatment are for the most part entirely sound, though we would have omitted the use of gauze packing as a means of induction of labor. We believe that unless a man is competent to use instruments he had better not perform the operation at all, because of the added danger of infection which the method under discussion undoubtedly causes, especially in the hands of the occasional operator. This restriction is, however, hardly fair, as there is good authority in favor as well as opposed to this method. The whole subject is admirably covered, and besides the chapters upon diagnosis, symptomatology, etiology, and pathology, the inclusion of which are, of course, predicted by the title, chapters have been included upon prophylaxis before and during pregnancy, operative technique, sepsis, and perforation. In addition, missed abortion, mole pregnancy, and therapeutic abortion, as well as ergot and its preparations, are discussed in an appendix of fifteen pages.

W. R. N.

SPONDYLOTHERAPY. SPINAL CONCUSSION AND THE APPLICATION OF OTHER METHODS TO THE SPINE IN THE TREATMENT OF DISEASE. By ALBERT ABRAMS, A.M., M.D., Consulting Physician to the Mount Zion and French Hospitals, San Francisco. 97 illustrations. San Francisco: The Philopolis Press, 1910.

THIS is rather a curious book which has not altogether repaid the time spent in its perusal. The following quotation from the preface may serve as an indication of the mental attitude in which the preparation of the book was approached. "The author was lead to a deeper study of spinal therapeutics in investigating various visceral reflexes which bear his name;" and further: "The successful

practice of spondylotherapy requires knowledge, observation, and experience of the highest kind." Turning to the end of the book, a bibliography of sixty-seven numbers is given, of which twenty-two are references to articles or books by the author. The subject appears to have some affinity with osteopathy and with the methods of one or two other schools. There are numerous tables selected, as a rule, from other authors, and some methods that appear to be distinctly original, particularly spondylography. Some of the statements appear to one not well versed on this subject rather sweeping. For instance, the painful centres, for the finding of which an ingenious method is given, are said to be so pathognomonic of certain ailments that the physician can almost make a diagnosis from the reflex centres involved. Another is that when one finds the spinal tenderness associated with some organic disease of an organ, as, for example, a gouty toe, or an ulcer of the stomach, if the area of spinal tenderness be frozen, the pain will disappear in the affected organ. If the freezing be repeated, apparently the ulcer or gout will get well, which is explained as follows: "Now, to the average physician it would be ridiculous that freezing over the area of tenderness was anything more than a palliative measure, yet sober thought endows analgesia with curative action." The reviewer hesitates to express his own thoughts upon this subject. This method is also effective, apparently, for persistent coughs.

Respiratory ataxia, a condition which has not received the attention the author believes it deserves, and which is capable of producing a remarkable group of symptoms, is thoroughly described. There is a very curious classification of the different types of back-aches, for one of which, at least, he accepts the uric acid etiology. He is an enthusiastic believer in the sinusoidal current. He holds that lumbar puncture will relieve headache due to an augmented intracranial pressure.

There is a description of a variety of pseudovisceral diseases which yield promptly to the freezing method. There is also a long chapter upon the forms of cardiovascular disease that can be relieved or cured by spinal treatment, including particularly cardiac insufficiency, the changes in tension of the bloodvessels, and even, apparently, aneurysm of the aorta. There are also sections on the respiratory and gastro-intestinal systems. The spinal methods of treatment are available in gastropsis, intestinal intoxication, constipation, and a variety of other conditions.

The author is apparently an enthusiast, but it is probable that a considerable portion of the medical profession will await more conclusive demonstration than the perusal of his book before adopting his methods generally. At any rate, the reviewer has the feeling that the elaborate series of visceral reflexes described has hitherto strangely escaped common medical knowledge. J. S.

GRUNDRISS UND ATLAS DER SPECIELLEN CHIRURGIE. By PROFESSOR DR. GEORGE SULTAN. Vol. II, pp. 624; 261 illustrations and 40 colored plates. *Lehmann's Medical Hand-Atlases*, Vol. xxxvii. Munich: J. F. Lehmann, 1910.

THE author apologizes for the long time (three years) elapsed since the appearance of the first volume of this popular work; but this delay has permitted him to include accounts of quite modern surgical methods only now coming into general use, such as arterial suture. Yet certain procedures are advised which many surgeons no longer regard as of value. Among such may be mentioned separate suture of the mucosa in intestinal anastomosis; irrigation in peritonitis; and the use of Bardenheuer's weight extension for fractures of the surgical neck and shaft of the humerus, the patient being confined to bed. There is no mention of Ruggi's inguinal method for the radical cure of femoral hernia; nothing is said of arthroplasty; and the section on chronic non-tuberculous arthritis is devoid of what little advances in classification and diagnosis have been secured by American surgeons. A bad prognosis is given for elbow fractures. In accordance with the plan of these *Hand-Atlases*, there is no attempt made to include pathology or etiology except as they bear directly on diagnosis; chief attention being given to symptoms and treatment. The first volume covered the head, thorax, and spine; while the present volume, larger by nearly 200 pages, includes the abdomen, male genito-urinary organs, and the extremities. The numerous illustrations are well chosen, and the colored plates unusually good.

A. P. C. A.

CONGENITAL DISLOCATION OF THE HIP. By J. JACKSON CLARK, M.B. Lond., F.R.C.S., Senior Surgeon to the Hampstead and North-West London Hospital. Pp. 92; 55 illustrations. London: Baillière, Tindall & Cox, 1910.

THIS is largely a personal record of the experience derived by the author from the manipulative treatment of forty cases of congenital dislocation of the hip. He gives entire credit for the development of the "bloodless" method to Lorenz (1895), damning with faint praise the pioneer work of Paci, in the following words: "There is no doubt, however, that the work of Paci had much influence in bringing about this great advance in surgery." Clarke, like many other surgeons, seems totally unaware that Lorenz as well as Hoffa was an early advocate of the "bloody" method, and that Paci "was publishing his work by the bloodless method from 1888 to 1893." "In 1894, at the International Congress in Rome, Lorenz and Hoffa came prepared to fight for their respective cutting operations,

but Paci by this time had systematized his work. He gave his results on 23 cases of congenital luxations, besides 5 of pathological and old traumatic ones; also those of ten other surgeons who had used his method. He submitted a specimen showing a perfect antemortem reposition, and wound up by performing his bloodless method on a patient before the assembled surgeons. The effect might almost be described as ludicrous. No more was heard of cutting operations. Lorenz, in the following year, modified Paci's procedure, and travelled far and wide exploiting it." (G. G. Davis.)

Among Clarke's 40 cases, he considers the results established in the first thirty patients. "These presented 39 dislocations, of which 18 were double and 21 were single; of the 18 double ones, 12 are cured and 2 are anteverted in a stable position, and 4 failed. Of the 21 single joints, 17 are cured, 1 is anteverted, and 3 have relapsed; the total being 29 out of 39 cured, 3 stable anteversions, and 7 failed." For cases which relapse, he has devised an operation consisting in incising the capsule posteriorly, elevating the periosteum and cotyloid ligament from the upper and posterior margins of the acetabulum, and pleating the capsule to these raised margins after reduction of the femoral head. This method he has employed successfully in 2 cases. For irreducible luxations he knows of no satisfactory treatment; beyond the slight relief to be secured from orthopedic apparatus, he regards these cases as hopeless. He seems to be unaware of the advances in the treatment of such cases inaugurated by G. G. Davis, Ludloff, and others.

A. P. C. A.

THE PSYCHOLOGY OF DEMENTIA PRÆCOX. By Dr. C. G. JUNG, Privat-Docent in Psychiatry in the University of Zurich. Authorized Translation, with an Introduction by FREDERICK PETERSON, M.D., Professor of Psychiatry in Columbia University, New York, and A. A. BRILL, Ph.D., M.D., Assistant in Psychiatry in Columbia University, New York. Pp. 153. New York: The Journal of Nervous and Mental Disease Publishing Company, 1909.

THIS is the third of the Monograph Series produced by the *Journal of Nervous and Mental Disease*. Its translators, Frederick Peterson, M.D., and A. A. Brill, M.D., while giving in their preface credit to Kräpelin for having introduced new life into psychiatry, insist that he only offered a general and superficial view of the subject and that he did not enter at all into psychology. The present work is the result of three years' experimental labor and clinical observation, and is along the same lines as Freud's well-known work on hysteria. In fact, the author admits that his attention was

drawn to the subject by the stimulation received from Freud's work. The subject matter is divided into five chapters and a conclusion. In the latter the author frankly admits that this work is simply a beginning, and is only an exposition of his own method of diagnostic association study in mental disease, and especially in dementia præcox. The last chapter is of special value, inasmuch as the author gives in detail his method of examining a case and the deductions at which he arrives. The work is well done, and should be read by everyone interested in mental diseases. T. H. W.

DE L'USAGE EN CLINIQUE DE L'ULTRA-MICROSCOPE EN PARTICULIER POUR LA RECHERCHE ET L'ÉTUDE DES SPIROCHETES. Par le DR. J. COMANDON, de la Faculté de Médecine de Paris licencié des Sciences. Paris: Steinheil, 1909.

To one who is using the dark field illumination for routine or special work this monograph will probably be of some service. It does not, however, bring to light many new facts of great interest and, therefore, must have a limited usefulness. The apparatus for dark field illumination is first described in sufficient detail, and then follows a number of chapters upon the use of this apparatus in the search for spirochetes in syphilis and the value of the method in the study of other forms of spirillosis. Certain observations upon the form and behavior of spirochetes in various fluids are reported, and the pamphlet ends with a study by the dark field illumination of a number of body fluids. W. T. L.

THE OPEN-AIR OR SANATORIUM TREATMENT OF PULMONARY TUBERCULOSIS. By F. RUFENACHT WALTERS, M.D., B.S., M.R.C.P., F.R.C.S., Physician to the Crooksbury Sanatorium, etc. Pp. 323; 29 illustrations and tables. New York: William Wood & Co., 1909.

DR. WALTERS prepared the book with a twofold object—that the first part be concerned with matters which an intelligent patient should know, and that the second part be concerned with the technical side for the assistance of the physician. Numerical references are made in many places in Part I to the more technical Part II. In the former there are several illustrations which show the proper methods of building floors, verandas, windows, shutters, screens,

etc., in sanatoria and improvised out-door shelters for consumptives. The subject of dietetics receives special attention by the presentation of about two dozen "useful recipes." Aside from the usual exposition of the technical side of tuberculosis, Part II contains a rather exhaustive table dealing with food values and their importance in tuberculosis. To the patient the subject in Part I is stated in a simple and thoroughly comprehensible manner; moreover, the illustrations lend attraction. However, one must take issue with certain statements relative to disinfection. It is well known that carbolic acid and bichloride of mercury are ineffectual in the disinfection of furniture and sputum respectively. To the physician the subject in Part II is presented systematically and comprehensively, though very briefly. On the whole, the book is meritorious, but one questions the value of adding Part II to a volume evidently prepared primarily for the guidance of the consumptive patient.

W. T. C.

REFRACTION AND MOTILITY OF THE EYE, WITH CHAPTERS ON COLOR BLINDNESS AND THE FIELD OF VISION, DESIGNED FOR STUDENTS AND PRACTITIONERS. By ELLICE M. ALGER, M.D., Adjunct Professor of Ophthalmology in the New York Postgraduate Medical School; Ophthalmologist to the New York Dispensary, etc. With 122 illustrations. Philadelphia: F. A. Davis Company, Publishers, 1910.

ABOUT two-thirds of this work is devoted to refraction and one-third to motility; the latter is the better. The author properly insists that the postgraduate student should master the principles (of optics and refraction) before entering a school; it is questionable whether the preliminary chapter upon optics is clear or full enough to be comprehended by self-study by one who knows nothing of the subject. As an acquaintance with the principles of optics is at the foundation of all further progress in understanding normal and abnormal refraction and accommodation, it is desirable to make this chapter as clear as the subject will possibly permit, even at the expense of many pages, illustrations of all kinds, and repetition if necessary.

Where extreme and contradictory views prevail the author wisely chooses a middle course. We could wish he were rather more emphatic upon the necessity of cycloplegics. The "two-thirds" rule in presbyopia, which is not mentioned at all, is surely superior to "ordering a convex glass strong enough to bring the near point to ten inches." We should like to see a reason for the author's preference for placing the light above the patient's head in the shadow test, rather than close to the mirror, which latter alone permits

practical coincidence of the point of reversal with the virtual source of light—an important detail which makes so strongly for accuracy. In directions for ordering glasses in hypermetropia we find no reference to allowance for range, but a series of rules, most of which we believe would fall away if the necessity of such an allowance were generally understood.

T. B. S.

SURGICAL ANATOMY. By JOHN A. C. MACEWEN, B. Sc., M.B., C.M., Senior Assistant to the Regius Professor of Surgery in the Glasgow University. Pp. 478; 61 illustrations. New York: William Wood & Co., 1910.

THIS manual of surgical anatomy is designed for the instruction of students of surgery and anatomy, and covers the matter usually embraced in a course on the subject. The volume, which is of quite modest size, is divided into five sections, discussing successively: (1) Head and Neck, Vertebral Column, Brain and Spinal Cord. (2) Thorax. (3) Abdomen and Pelvis. (4) Lower Extremity. (5) Upper Extremity. The illustrations are few in number, but well selected, and serve well by their diagrammatic, if not always artistic, clearness to inculcate the salient points accentuated in the text.

It is perhaps hypocritical to wish that an author who writes upon surgical anatomy should have written instead upon applied anatomy; but the student and practitioner so often look for the practical application of anatomical facts in text-books on surgical anatomy, and fail to find just what they want, that we wish the author of the present volume had paid more attention to the applied aspects of his subject, and less to regional anatomy. This is not meant to imply that there are no practical applications, for there are numerous such, and very excellent too; but he has not, we venture to suggest, a just appreciation of the distinction between applied and merely surgical anatomy. There are many excellent text-books and manuals upon the latter subject, but a work of the highest type on applied anatomy has yet to be published.

There are a few typographical errors (*e. g.*, *visci* for *viscera*, p. 148; *errigentes* for *erigentes*, p. 183; *eighth* for *eighteenth*, p. 402, line 3) which do doubt will be corrected in another edition; and the use of the term *incontinence* (p. 148) of urine and feces, when in reality *overflow* is intended, will perpetuate confusion in students' minds as to the effects of lesions of the spinal cord above and below the lumbar enlargement, in which are the centres for the bladder and rectum. The distinction to be drawn is that in damage to the cord *above* these centres there is overflow of urine and feces, as the voluntary impulses cannot reach the spinal centres, with the result that

the centres act automatically (a common phenomenon); whereas if the centres themselves, or the nerves between them and the bladder or rectum are damaged, then there is true *incontinence* (very rare).

A. P. C. A.

MAMMALIAN ANATOMY, WITH SPECIAL REFERENCE TO THE CAT.
By ALVIN DAVISON, Ph.D., Professor of Biology in Lafayette College. Second edition. Pp. 246; 114 illustrations. Philadelphia: P. Blakiston's Son & Co., 1910.

THE author states that "when the first edition of this book was published, less than a half dozen medical schools in the United States required the entering student to have any knowledge of the structure of the lower animals. To-day a knowledge of mammalian anatomy or zoölogy is considered one of the first requisites for entering upon an intelligent study of medicine." To meet such requirements the present volume appears to be well adapted; and it may also be found useful, as the author suggests, to the student of psychology and teachers of elementary physiology in high schools. In the present edition the BNA nomenclature has been cautiously introduced; and new figures and a glossary have been added.

A. P. C. A.

L'HYPOPHYSE ET LA MÉDICATION HYPOPHYSIAIRE. By ARTHUR DELILLE Pp. 336. Paris: G. Steinheil, 1909.

THIS monograph considers the functions and pathology of the pituitary as determined by a series of experimental and clinical studies, executed under the direction of L. Renon, and extending over a period of three years. The first part of the book takes up the anatomy, histology, physiology, and chemistry of the hypophysis and its secretion; the second part is devoted to experimental researches, in which the action of extracts of pituitary is considered in relation to various physiological processes; the third part deals with clinical observations and observations of the effects of the administration of extracts of pituitary in different diseased conditions; and the fourth part discusses the indications for medication with pituitary extracts.

This contribution to a subject but little understood represents much careful work, especially along experimental lines, and the subject matter is presented in a concise and conservative manner. Some of the most important conclusions of the author are as follows:

Histology demonstrates that the anterior lobe of the pituitary body possesses decided glandular activity, and the posterior lobe is devoid of such activity. On the contrary, experiments prove that the extract of the posterior part is physiologically active, and that of the anterior portion gives no apparent results. The extract of the posterior lobe (or of the entire gland) causes elevation in arterial tension and vasoconstriction, less accentuated than that from the use of suprarenal extract, but of longer duration. On the kidneys, the effect is at first vasoconstriction, but later vasodilatation and diuresis. Physical development and intelligence are stimulated, thyroid activity is diminished, and suprarenal function is increased. Clinical observations practically coincide with experimental results and pituitary administration is suggested in conditions presenting low arterial pressure, tachycardia, sensations of heat, profuse perspiration, oliguria, anorexia, asthenia, insomnia, arrested development, etc. It is also recommended that the daily dose should not exceed one-half of a fresh gland of the beef or its equivalent.

S. D. I.

A TEXT-BOOK OF PATHOLOGY. By JOSEPH MCFARLAND, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia. Second edition (pp. 956); 437 illustrations. Philadelphia and London: W. B. Saunders Co., 1910.

A TEXT-BOOK UPON THE PATHOGENIC BACTERIA. By JOSEPH MCFARLAND, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia. Sixth edition (pp. 709); 211 illustrations. Philadelphia and London: W. B. Saunders Co., 1910.

DR. MCFARLAND'S two books—the one on *Pathology*, the other on the *Pathogenic Bacteria*—have become standards in their respective fields, so that it becomes necessary only to discharge the pleasant duty of recording the publication of new editions. Both books have been considerably revised; the results of recent studies and investigations and the real additions to our knowledge in pathology and bacteriology have been incorporated. Both, therefore, may be highly commended as representative of present-day knowledge of the subjects of which they treat. Perhaps some day Dr. McFarland will add to his book on the *Pathogenic Bacteria* a section on the pathogenic zoöparasites, the pathogenic as well as economic importance of which is becoming almost daily increasingly manifest.

A. K.

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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A New Sign of Inflammation of the Meninges.—SIGNORELLI (*Rivista Critica di Clinica Medica*, 1910, No. 15) describes the so-called retro-mandibular tender point as a constant sign of meningitis. This point is located behind the superior extremity of the inferior maxilla, below the lobule of the ear, and in front of the mastoid process. In healthy individuals this point is sensitive, but in cases of meningitis pressure with the index finger elicits extreme pain and provokes contractions of the facial muscles: it is apparently the trunk of the facial nerve which is sensitive. The sign is present throughout the attack. It often precedes the stiffness of the neck and the Kernig sign. In tuberculous meningitis the muscular contractions, after pressure at this point, occur even when the patient is paralyzed and comatose.

Chronic Antimony Poisoning in Typesetters.—SCHRUMPF and ZABEL (*Archiv f. exp. Path. u. Pharm.*, 1910, lxi, 242) have had the opportunity of observing a large number of typesetters during the last year or more, and were struck with the variety of lead poisoning among them. Many of the typesetters, however, exhibited a clinical picture characterized by a tired expression of the face, complaints of nervousness, irritability, insomnia, exhaustion especially in the morning, vertigo, headache, general and local muscular pains, neuralgic pains in the extremities, nausea and a tendency to vomit, with disturbance of the stomach and bowels, constipation. Varying degrees of intensity were observed. The majority of those affected were young workmen between the ages of fifteen and thirty-five years, who had been employed as typesetters for periods of one-half to thirty-one years. Schrumpf and Zabel were at first inclined to regard their symptoms as manifestations of

plumbism. They found, contrary to the rule in lead poisoning, that the blood pressure was not elevated, that the blood contained no basophilic granules, nor was there leukocytosis, and that no albumin or bile pigment could be detected in the urine. In fact, the blood pressure, they say, was rather low, there was leukopenia with a marked eosinophilia (10 to 25 per cent.), there were no basophilic granules in the red cells, though slight polychromatophilia was seen, and in one case a few normoblasts, and the urine was normal. In typesetters without any complaints, and in whom physical examination revealed no organic disease, the blood was normal, except for moderate increase in the eosinophilic cells (up to 9 per cent.). They concluded, therefore, that a diagnosis of lead poisoning was not justified. On inquiry, the authors found that the mixture used in covering the type contained lead, 70 to 80 per cent., tin, 5 per cent., and antimony, 15 to 20 per cent. As tin is of no importance toxicologically, their attention was directed to the antimony. Experiments on rabbits showed that antimony causes a rather marked reduction in the number of leukocytes, with an eosinophilia up to 25 per cent; no other changes were found in the blood. (Arsenic, which is an impurity often present in antimony, caused some leukopenia, but the effect was less marked than with antimony.) With Marsh's test, an antimony mirror was obtained from the feces of the poisoned rabbits. Schrumpf and Zabel then examined the stools of their patients, and in two of them they obtained an antimony mirror, removing practically all doubt as to the nature of the intoxication. The prognosis of the condition is good. Absence from work for two or three weeks, with a milk diet and exercise, sufficed to relieve the symptoms in the majority of instances. After leaving their employment there was an increase in the number of leukocytes in the patients' blood.

The Treatment of Malaria with "606."—WERNER (*Deut. med. Woch.*, 1910, xxxvi, 1792) has used "606" in 22 cases of malaria (11 each of tertian and estivo-autumnal fever) which were resistant to quinine. With 0.6 to 0.7 gram of "606" the tertian fevers are apparently cured. The estivo-autumnal infections proved resistant to the remedy; the asexual forms disappeared temporarily from the blood, but reappeared in about six days in one-half of the cases. The drug acts in about twenty-four hours. Werner recommends "606" in those cases in which the parasite is resistant to quinine and also in patients who are intolerant of quinine. He recommends that the dose, 0.6 gram, be given in part subcutaneously and the remainder intravenously.

A New Method of Administering "606."—KROMAYER (*Berl. klin. Woch.*, 1910, xlvii, 1698) has devised a new method of administering "606" which has some obvious advantages. He takes 3 grams of "606" and rubs it in a mortar with liquid paraffin until the drug is in a finely divided state. It is then transferred to a glass-stoppered bottle of 50 c.c. capacity, and liquid paraffin is added to make the volume 30 c.c., so that 1 c.c. equals 0.1 gram of "606." It should be kept in the dark. Before using, the suspension must be shaken until no sediment remains at the bottom of the bottle. The needles for injection should be of wider bore than those usually employed in giving mercury salicylate, and are best kept in a Petri dish in fluid paraffin. They must, of course, be sterilized

each time before using. The injection must be made very slowly to avoid tearing the tissues. Kromayer has used this method in 100 cases without a single instance of pain or local swelling. Ambulant cases may receive the injection unless there are definite contraindications. Clinical results indicate that the arsenic is rapidly absorbed and urinary examination confirms this view.

The Treatment of Strychnine Poisoning by Insufflation and Curare.—SHAKLEE and MELTZER (*Berl. klin. Woch.*, 1910, xlvii, 1776) find that 0.4 mg. strychnine per kilogram of body weight is invariably fatal to dogs, death being due to asphyxia from spasm of the respiratory muscles. They have employed insufflation and curare in the treatment of experimental strychnine poisoning in dogs. The animals were given 0.5 to 1 mg. per kilogram; 0.9 to 1 mg. always proved fatal. With doses of 0.8 mg., twice the lethal dose, recovery of the animals was obtained in 13 of 22 instances. The only visible sign of life in the animal was the heart beat. The dose of curare employed was 1.5 mg. per kilo. Infusion of Ringer's solution hastened the elimination of both strychnine and curare. Shaklee and Meltzer suggest this treatment in suitable cases of poisoning in man. The surviving dogs were sacrificed at the end of a few weeks or months, and showed no ill effects from the insufflation in the trachea, bronchi, or lungs, though the experiments lasted three and one-half to seven hours.

The Effect of Malignant Tumors upon the Blood.—BARADULIN (*Folia Hæmatol.*, 1910, ix, 407) reports a careful and detailed study of the blood of 72 patients suffering with cancers in various parts of the body, and of 16 patients with sarcomas. He has summarized the findings in the carcinomatous patients, grouping the cases according to the location of the newgrowth in the body. In the general summary of all cases of carcinoma the following facts are emphasized (the individual summaries possess greater value but would require too much space): (1) Decrease in the hemoglobin is proportionate to the cachexia; in many cases it sinks to an extremely low point. The decline in hemoglobin is also dependent largely on the location of the cancer. The size of the tumor is without influence and its duration is also of little moment. Tumors which do not interfere with the respiration or digestion may grow for months with little or no reduction in hemoglobin. (2) The number of erythrocytes is decreased, but to a less extent than the hemoglobin, so that (3) the color index is below 1. (4) In the later stages of cancer of the internal organs, microcytes, macrocytes, and poikilocytes appear. They are the more numerous, the severer the cachexia. Nucleated red cells with polychromasia may be seen. (5) With slowly growing neoplasms, leukocytosis is slight or is missed altogether. On the contrary, rapidly growing tumors cause leukocytosis, with increase of the polymorphonuclears and lymphocytes in the earlier stages, later in the disease, of the mononuclears. Those tumors which ulcerate, become infected, and lead to hemorrhage, present leukocytosis with increase of the mononuclears. (6) The specific gravity of the blood is lowered in proportion to the diminution in hemoglobin and red count. (7) The alkalinity is reduced with rapidly growing tumors. With sarcomas there is moderate anemia with low color index. Leukocytosis

was observed in all cases. Sarcoma of the soft parts occasions an increase of the polymorphonuclears at the cost of the lymphocytes. In lymphosarcoma, the condition is just reversed. Bone sarcoma is accompanied by increase of transitionals and eosinophiles, with decrease of polymorphonuclears. Myelocytes are found. The specific gravity and alkalinity are little affected.

Malarial Pigment.—**ASCOLI** (*Polichinico*, 1910) says that the pigment found in the spleens of individuals dying of pernicious malaria presents the same picture as that seen in the spleens of animals poisoned with pyrodine. The pigment gives the spectrum and chemical reactions of hematin, into which the endoglobular parasite converts the hemoglobin. The hemoglobin content of an infected red blood corpuscle depends upon the variety of the hematozoön which it harbors and not upon the amount of pigment produced. The pigment is formed particularly in the spleen and bone marrow, where the parasite undergoes the last phases of the asexual cycle and a large part of the sexual phases. It persists in the liver and spleen and causes an inflammatory reaction. It disappears quite quickly from the general circulation.

Intestinal Amœbiasis.—The prevalence of amœbic infection of the colon, according to **MUSGRAVE** (*Philippine Journal of Science*, 1910, v, 229), is of sufficiently frequent occurrence to deserve careful consideration. Fifty fatal cases form the basis of his report. In no one of these was looseness of the bowels a symptom at any time. Indeed, constipation was the feature. At autopsy, however, characteristic amœbic lesions were present in all 50 cases. The lesions varied from those just beginning to those showing ulcers and extensive destruction of the mucous membrane. General symptoms varied greatly, though not pathognomonic, yet strongly suggestive of amœbic infection. Abdominal "aching," more or less general, worse at night and the early morning, and often accompanied by flatulence, is the most frequent symptom. Distention and constipation are common. Loss of weight generally becomes noticeable. Excessive perspiration quite frequently brings the patient to a physician. Looseness of the bowels, as a dysentery or diarrhœa, has long been the strong diagnostic point, but facts show it also to be a very unreliable one. If the ulceration is low, the sigmoidoscope gives valuable help. There is but one constant finding, and that is the presence of amœbæ in the bowel discharge. **ROGERS** (*Ibid.*, 1910, v, 219) emphasizes the relation of intestinal amœbiasis to tropical liver abscess. In his experience in Calcutta, 57 out of 63 cases of liver abscess have had a clinical history or postmortem evidence of dysentery. In 45 fatal cases of liver abscess, only 1 failed to show the lesions of amœbic dysentery or old scars at the autopsy. In the wards of the European General Hospital at Calcutta, 43 out of 50 cases of liver abscess gave histories of either dysentery or diarrhœa. Finally, the author's experience with ipecac in the presuppurative stage of liver abscess and in the post-operative stage warrants recommendation.

Test for Gastric Cancer.—The glycytryptophan test of Neubauer and Fischer for cancers of the stomach has already been recorded in this JOURNAL, as well as the modifications in its application suggested by

Lyle and Kober. The test depends upon the presence of a peptid-splitting ferment in the cancerous gastric juice. Incubation of the dipeptid glycytryptophan and the ferment (the filtered gastric juice) for twenty-four hours results in the production of simple tryptophan, easily demonstrable with bromine water. Neubauer and Fischer emphasized that tryptophan may be present beforehand in the stomach contents; that blood contains a similar ferment and its presence must be ruled out; that trypsin in the stomach juice will accomplish the same cleavage, and bile is indicative of its presence. Lyle and Kober drew attention to variability in results, and required two out of three tests positive before interpreting the results. To avoid having duodenal contents in the stomach, the patients were purged at night, kept upright in the morning, and the test meal given at noon. WEINSTEIN (*Jour. Amer. Med. Assoc.*, 1910, lv, 1085) recommends making use of the ferment's ability to produce tryptophan in the stomach itself. Four or five hours after a meal of bread and butter, meat plainly prepared without extra seasoning or dressing, and some very sweet, weak tea, stomach contents are secured, filtered, and tested with bromine water for tryptophan. If present, the reaction is positive. If absent, the filtrate in a stoppered bottle with or without toluol is incubated for twenty-four to forty-eight hours, and again tested. The most serious defect is inconstancy. If three or four tests are negative, the case is probably non-cancerous. Weinstein does not recommend preservatives. They interfere with a sharp bromine test, and the influence of peptid-splitting bacteria is too slight to need consideration. Blood that is not grossly visible will not contain enough ferment to confuse the results. And the author believes that occult bile could hardly be accompanied by sufficient trypsin to produce a detectable amount of tryptophan in the test. After all is said, one fact stands out prominently: That the test yields positive results in practically all cancer cases and hardly ever in others, as may be seen in the results by Neubauer and Fischer, Lyle and Kober, and Weinstein.

A Comparison of the Results Obtained with the Different Sphygmometers.
—AMBLARD (*Archives gén. de méd.*, Paris, 1910, iii, 513) draws attention to the fact that the many instruments for measuring arterial tension are based upon four principal methods, namely: (1) Compression of the artery by an ampulla (Bach); (2) compression by a band (Riva-Rocci); (3) compression of the finger by a ring (Gaertner); and (4) the oscillatory method, indisputably preferable and totally different from the others. The difference in standards for normal individuals depends upon the difference in the instruments, and upon the fact that some measure the maximal arterial pressure, some the minimal, and others the arteriole tension. The sphygmometers of Bach, Potain, Sable, Riva-Rocci, and the sphygmo-signal of Vaquez all indicate maximal pressures. Comparative records show that there is absolutely no parallelism which can be established *a priori*; whereas the normal pressures with one of these methods may be about 30 mm. of mercury higher than those of a second method, in measurements of hyper- or hypotensions no such corresponding relation exists. The differences between the Potain and Riva-Rocci sphygmometers in a normal individual may be from 20 to 30 mm.; in pathological conditions they vary from 10 to 100 mm.

On the other hand, Amblard found that the instruments recording minimal pressures (the sphygmometer of Hill and Barnard, Amblard's sphygmometroscope, Lagrange's pulsocardioscope, and the oscillometer of Pachon) furnish comparable and parallel results. It is impossible to establish a parallelism between the results furnished for the maximal tension by the different methods, which in itself is reason enough against looking for any correlation of these same results with those furnished by other instruments. It is advisable to compare only those results obtained by the same instruments; and the recognition of the one or the other tension is equally indispensable for an appreciation of the conditions of the arterial circulation. Finally, Amblard found that the method of Gaertner, compression of the finger with a ring, gave almost identical results as the Riva-Rocci. It demonstrated that the pressure in the arterioles is practically the same as the maximal tension.

The Influence of the Position of the Body upon Evacuation of the Stomach.—PERUSSIA and MARKOVICZ (*Gazz. med. italiana*, March 31, 1910) demonstrate the value of radiological examination of the motor function of the stomach when the patient is placed in the left and right lateral (prone) positions. For instance, a little difference in the time of evacuation in the two positions, a rapid emptying in both left and right positions, points to hypermobility. In atonic motor insufficiency, the left lateral position retards enormously the time of evacuation, whereas the right accelerates it markedly. The difference in the two positions is very great. In motor insufficiency due to pyloric stenosis, the left position retards the emptying less than it does in atonic insufficiency. The resulting hypertrophy compensates somewhat for the stenosis. But in contrast, the right position does not hasten the evacuation. The cause of the insufficiency, the obstruction, persists. In this case the difference in the two positions is slight. Perussia and Markovicz emphasize the advantage of the right lateral position in cases of atony of the stomach, as well as the disadvantage of the left.

SURGERY.

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Circular and Lateral Suture of a Vein.—ZAAIGER (*Zentralbl. f. Chir.*, 1910, xxxvii, 1283) has performed several autoplasmic and homoioplasmic kidney transplantations in dogs, and has one dog which has lived more than two years with the left kidney transplanted to the inguinal

region and the right kidney extirpated. There are, however, a number of difficulties in the technique which, with biological troubles, cause failures in these experiments. One of these technical difficulties lies in the vein suture. Zaaiger often found at autopsy on the animal that a thrombosis had developed at the vein suture, while the arterial suture was faultless. One of the chief principles of vessel suture is the adaptation of the endothelial surfaces which is to be obtained by turning out the intima as much as possible. This is much more easily done with arterics than with veins. By the methods of Carrell and Stich the retained sutures penetrate the wall of the vessel only once, and after turning out the intima as much as possible they are knotted. Zaaiger, in introducing his retaining sutures from the intimal side into each end of the divided vessel, passes them under the intima and out again as in a transposed Lembert suture. When the knot is tied the intima is spontaneously and easily turned outward, so that the remaining sutures can be introduced without further attention being paid to the turning out of the intima. By this method a circular suture of the vena cava of a dog was carried out and an absolutely ideal result obtained. The following method of applying a lateral suture to a vein was employed in a case of cancer of the penis with adhesion of cancerous nodes to the femoral vein: The adherent mass was drawn upon so that the wall of the vein was brought to a point, where it was ligated. A suitable forceps was then applied on the vessel side of the ligature, approximating the two walls of the vein. On the vessel side of the clamp a suture was passed from one side to the other through the two walls of the vein and tied at both ends. The forceps was then removed and the mass together with the diseased portion of the vein cut away. The part of the vein contused by the forceps was then turned in by a continuous suture. Endothelium was thus approximated to endothelium and the blood stream in the main vessel was uninterrupted. A good result was obtained.

An Explanation of the Pathogenesis of Appendicitis Based upon Experimental and Bacteriological Investigations.—HEILE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1910, xxii, 58) has undertaken to study, particularly, why, in so many cases, appendicitis becomes localized, and why, in many cases, it becomes a dangerously progressive inflammation. For several years he has been attempting the solution of the question by bacteriological examinations, but, like others, he has not met with much success. Better results have followed animal experimentation. Simple ligation of the appendix in dogs was followed by the reestablishment of the canal of the appendix after the suppurative division of the wall and the separation of the constricting silk ligature. If, peripherally to the ligature, a paraffin plug was introduced into the lumen of the appendix, then the peripheral portion remained closed and the canal was not reestablished. This gave rise to impairment of the health of the animal. It did not cause peritonitis or death, but only a circumscribed inflammatory process, which was followed, after weeks, by adhesions of the omentum and neighboring coils of intestines. The portion of the appendix peripheral to the ligature became more or less dilated and filled with more or less abundant leukocytic contents (hydrops or empyema), usually with numerous bacteria, which, how-

ever, did not produce a progressive inflammation. The tissues of the surrounding wall, on the contrary, showed a slight difference from the normal histological picture, and after a few weeks only here and there a round-cell infiltration. If a portion of the appendix containing normal feces is ligated with silk, and injected with paraffin, then there develops from the feces a chemical and bacteriological infection of the wall, which, very much like the same type of appendicitis in man, proceeds to destruction of the wall and the development of a diffuse, suppurative, ichorous peritonitis and death of the animal, according to the severity of the infection, in from one to five days. The pathologico-histological picture of the destructive inflammation is characterized by two typical courses. In the first there is a localized epithelial defect, which is accompanied by a rapidly progressing suppurative lymphadenitis of the intestinal wall. The abundantly developed tissue of the lymphoid follicles favors this process very much. In the first few hours after the beginning of the inflammatory process, there develops on the peritoneum, by extension through the lymph paths, an extensive layer of exudate (containing bacteria, leukocytes, and fibrin), although on the mucous surface there can be found only a very small defect. In the second type the excessive development of chemicobacteriological toxins does not result from the primary inflammation and advancing lymphangitis, but from the excessive necrosis, first, of the mucosa, then of the rest of the wall, until perforation occurs into the peritoneal cavity. The course of the process will be favored by the increasing fecal and paraffin contents, because the progressing inflammation is producing exudation in the interior of the lumen and the separation of the portions of the tissues, which adds to the pressure that is to produce the perforation of the badly diseased appendiceal wall. The changes in the blood-vessel walls are of great importance in the course of the destructive inflammation. Either there develops a hyperemia, as from a hemorrhagic infarct, or there occurs an anemic, necrotic infarct. It may be said with certainty that vessel changes are not necessary for the origin of the inflammation. For the origin of the destructive appendicitis, of the very greatest importance, is the retention of feces in the closed end of the appendix. Bacteria alone never produce a destructive inflammation.

Anuria after Gallstone Operations.—CLAIRMONT and HABERER (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1910, xxii, 159) call attention to cases of severe gallstone disease with common-duct obstruction or cicatricial stenosis, in which, at the conclusion of the operation, there develops dangerous oliguria or fatal anuria. These severe disturbances of the urinary secretion are to be traced to parenchymatous degeneration of the kidneys, which, aggravated by the effect of the damage to the liver parenchyma, are overcome by the influences of the operation and narcosis. A complete anuria is accompanied by an exhaustion of the biliary secretion, due to an inhibition of the liver function. The disturbance of the kidney function is not dependent upon any single factor, such as the long-continued jaundice, alone, but is due to the combination of all the factors resulting from the severity of the disease. Individual predisposition appears to play a certain part. Clairmont and Haberer emphasize that, according to their observations,

all kidney symptoms may be absent, and that in individual cases, from the surgical side, a definite prognosis cannot be given. These accidents in gallstone disease can be provided against only by operation before severe liver disturbances develop. The specific damage to the parenchymatous organs that results from extensive operations, long-continued narcosis, and anemia are to be avoided as far as possible. Conditions entirely similar to those observed clinically in men can be produced experimentally in dogs.

The Mobile Cecum as a Cause of Many Cases of Chronic Appendicitis.—STIERLIN (*Deut. Ztschr. f. Chir.*, 1910, cvi, 407) bases his extensive study of this subject upon 61 cases upon which Wilms did the operation of cecopexy. Twenty-five per cent. were in males and 75 per cent. in females. Sixty-seven per cent. were between the ages of fifteen and twenty-five years. In most of the cases the diagnosis of a mobile cecum was based upon the following symptoms: (1) Periodic attacks of colicky pain, localized chiefly in the region of the cecum and ascending colon, generally without fever, often associated with long-continued pain in this region, and not rarely in the region of the stomach. The attacks of colic occurred in 86 per cent. of the cases. (2) Chronic, usually severe, constipation, occasionally alternating with brief periods of diarrhoea, and particularly at the conclusion of an attack of colic. Severe constipation occurred in 77 per cent. of the cases. (3) In the region of the cecum is a distended tumor, which is distended by gas, and on palpation is soft and gurgling, is painless or somewhat tender, and shows considerable mobility. In all cases the diagnosis was established by the x-rays, which determined the abnormal mobility of the cecum, its size and atony, and the diminished motor function. The permanent results in 43 cases were: 75 per cent. cured, 16 per cent. improved, and 9 per cent. unimproved. In 9 cases of long mobile cecum with the typical symptom-complex, appendectomy without cecopexy gave the following results: 2 cured (with persisting constipation), 3 improved, and 5 unimproved. An abnormally long cecum, in rare cases, through kinking and rotation, may lead to severe clinical disturbances. The clinical picture of a mobile cecum develops when, besides a long cecum, there is also a primary or a secondary atony of the colon, or other cause of stoppage in the large intestine, as at the splenic flexure. Atony of the colon or cecum may be congenital, it may be due to a chronic colonic constipation, to an abnormal situation of the colon, or to a combination of these factors. The chronic constipation is most frequently due to a mobile cecum. The colicky attacks of pain and the continued pain in the intervals are due to the pull on the mesentery of the overdistended cecum and, in consequence of the constipation and probably also antiperistalsis, the outward displacement of the cecum. It is probably also due to the effect of the distention on the sensitive nerves in the cecal wall.

Concerning the Value of a Simple Continuous Suture Passing through the Whole Vessel Wall.—SCHILLER and LOBSTEIN (*Deut. Ztschr. f. Chir.*, 1910, cvi, 487) say that a simple continuous suture passed with the aid of retaining sutures is well suited for the anastomosis of vessels, and that the operation is easily carried out. The finest silk and a thin

needle are employed. With the strictest asepsis, favorable results were obtained in 40 per cent. of the arterial sutures and in 60 per cent. of those in veins. In the most severe wounds of the vessels, with loss of vessel substance—up to 2 cm.—by means of a simple circular suture, a favorable result was obtained. When the loss of vessel substance is greater than 2 cm., vessel transplantation is to be preferred. Suture of the smaller arteries gives a relatively better result than of the veins, since in the larger arteries, because of the blood pressure, the suture will be insufficient. It tears out and causes a secondary hemorrhage. Suture of the larger veins gives a better result than of the smaller, since the latter easily thrombose. A completely favorable functional result was obtained in more than 40 per cent. of the cases in which longitudinal vessel wounds were closed by a continuous suture, and in those in which a circular suture was employed after a transverse division of the vessel, as in resections—the loss of vessel substance being less than 2 cm. No aneurysmal formation was observed up to six months after the operation by this simple suture method.

Cancer of the Prostate.—YOUNG (*Ann. d. mal. d. org. gén.-urin.*, 1910, ii, 1742 and 1840) reports an elaborate study of 111 cancers of the prostate, nearly all personal cases, or examined by Young. Two were below fifty years of age; 25 were from fifty to fifty nine-years; 50 from sixty to sixty-nine years; 17 from seventy to seventy-four years; 13 from seventy-five to seventy-nine years; and 4 from eighty to eighty-four years. Carcinoma of the prostate is more frequent than is generally supposed. It was found in 20 per cent. of prostates increased in volume. In 500 cases of urinary obstruction, 400 were due to simple hypertrophy, and 100 to carcinoma. The symptoms were, in general, the same as those of hypertrophy, but the pain, local and radiating, simulates often that of other affections (renal, spinal, and sciatic) and is often the principal symptom. Carcinoma can begin by a small nodule in a prostate otherwise healthy, or one presenting a chronic prostatitis. A simple hypertrophy may become the seat of cancer, but usually in a non-hypertrophied region. It occurs more frequently in the posterior subcapsular region, behind the hypertrophied lateral lobes. Cancer remains localized a long time within the prostate, the ureter, bladder, and posterior capsule resisting invasion a long time. The periprostatic invasion begins generally along the ejaculatory ducts in the space above the prostate, between the seminal vesicles and the bladder and above the aponeurosis of Denonvilliers. The cancer generally reaches the inferior surface of the trigone and the lymphatics which extend toward the walls of the pelvis. The pelvic nodes, however, are involved late, and often the affection attacks the bone before the nodes. Examination of the prostate and seminal vesicles ought always to be practised, and when the prostate is found to be hard or only an indurated nodule in a man past forty-five years of age, cancer ought to be suspected, especially if there is no history of prostatitis, and if there is no hypertrophied lobe projecting into the bladder. In these cases, even if there are few symptoms, an exploratory operation should be done, and if the appearance alone of the posterior surface of the prostate does not suffice for a diagnosis of cancer, it will be necessary to make an immediate examination, microscopically, by the freezing method, of small pieces removed

from the lateral lobes. If the lesions are cancerous, the incision made should be cauterized, and a radical operation performed. A cure can be obtained only by a systematic excision of the seminal vesicles, the vasa deferentia, and the anterior two-thirds of the trigone. The operation is neither difficult nor dangerous, and a permanent cure has been obtained by this procedure (five years elapsing after the operation). When the disease is advanced and urination difficult, it will be necessary to catheterize the patient frequently. When catheterism is difficult or painful, a palliative operation will be necessary; in some cases suprapubic cystotomy. Excellent results, however, in combating the obstruction and vesical pain have been obtained by conservative perineal prostatectomy.

Transthoracic Cardiotomy, a New Method for the Cure of an Impassable Cicatricial Stricture of the Œsophagus.—FISCHER (*Zentralbl. f. Chir.*, 1910, xxxvii, 1393) offers an operation which he says will succeed in those cases in which all other methods of cure have failed. In a boy, aged three years, with an almost impassable stricture of the Œsophagus, the stomach was opened for the purpose of performing a gastro-enterostomy, when it was found to be the seat of an hourglass constriction. This was removed by the pyloroplastic operation of Heineke-Mikulicz. A Kader gastrostomy, with Senn's modification, was performed, and to place the stomach at rest a tube was passed through the pylorus into the duodenum. A skiagram taken after the operation showed a stricture of the Œsophagus extending from the bifurcation of the trachea to within 2 cm. of the diaphragm. A fine, thread-like shadow showed that the bismuth had passed the stricture. Various attempts to pass the stricture by silk thread and other means from above and below failed, and the child was being nourished poorly through the gastric fistula. Under continuous insufflation of the lung by the Meltzer-Auer method, the thorax was opened in the seventh intercostal space and the ribs separated. As the opening proved to be too high, a second was made in the eighth space, which gave easy access to the diaphragm and lower part of the Œsophagus. The lung was retracted by silk cloths sterilized in vaseline. The pleura covering the Œsophagus was divided, the vagi were pushed aside, the Œsophagus freed from its bed and wrapped in gauze. The Œsophagus was then separated from the diaphragm with a blunt forceps and the peritoneum drawn through, and with it the stomach, into the thoracic cavity. The stomach was easily drawn up to about 7 cm. from the entrance of the Œsophagus. The pleural cavity was carefully packed off with the silk cloth already mentioned, and the cardia divided between two suture retractors transversely, about 3 cm. below the Œsophageal opening. A ureteral catheter with a mandrin was passed easily through the stricture and out of the mouth, where it was secured with an arterial clamp. A suitable forceps was then passed through the gastro-enterostomy opening to the incision in the cardia, where it seized the lower end of the catheter and drew it out of the stomach fistula. The incision in the cardia was closed by silk sutures in a double row, the stomach returned to the abdominal cavity, and the Œsophagus fixed to the diaphragm and peritoneum. The thoracic wound was closed and a dressing applied. The patient withstood the operation well, but through a failure in the technique the

patient received an overwhelming and concentrated dose of ether and collapsed. He died twenty-four hours after the operation. Fischer looks upon it as a useful and simple operation.

Saccular Autoplasty in Necrosis of the Intestine from Strangulated Hernia.—LERDA (*Zentralbl. f. Chir.*, 1910, xxxvii, 1339) calls attention to the restricted field for the employment of the omentum in reinforcing sutures in the intestine, or in circumscribing an abdominal organ. The peritoneum has also been used for similar purposes, but not in strangulated herniæ, where it is useful and its technique simple. Often the strangulated portion of the bowel is of doubtful vitality, and is either distinctly necrotic or has already been perforated. Only in the more advanced cases has the gangrene extended to the whole strangulated loop. Generally, the necrosis is limited to the constricted hernial ring, while the remaining portion of the involved bowel is merely the seat of a passive hyperemia. In such cases the choice of operation lies between resection of the suspected intestine, the formation of an artificial anus, or a turning in of the necrotic portion, which is rarely possible, on account of the disturbances in nutrition in the neighboring tissues. In a severe case of strangulated hernia in a woman, aged seventy-four years, Lerda, after so incising the sac as to make a movable flap from it, applied the external surface of this flap over the necrotic band and sutured its free end to the mesenteric attachment of the bowel. An iodoform tampon was introduced into the hernial ring and the wound closed. A fecal fistula resulted. The first stool occurred on the twelfth day, and after that about every second day. On the thirty-fifth day the patient left the hospital with a fistula which would hardly admit a probe. In a second case the same operation was performed, with the exception that instead of the external or bloody surface of the sac, the internal or endothelial surface was applied to the intestine. This patient had a stool on the third day, and regularly afterward. On the sixth day a fecal fistula developed, but it was completely closed twenty-three days after the operation.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Treatment of Syphilis with "606."—IVERSEN (*Munch. med. Woch.*, 1910, lvii, 1723) substantiates results of other observers with his experience at St. Petersburg with 60 patients. He found the intravenous injections more satisfactory. He says that they are less painful than intramuscular injections and, furthermore, enable a more accurate dosage. In addition their action is more rapid and the dose required is smaller. He says that intravenous injection of "606" is usually followed in two or three hours by a chill lasting half an hour, accom-

panied by a rise of temperature, frequently by pains in the limbs, and in some cases by vomiting and fluid stools. The next day the patient feels well except for some weakness. He found spirochetes constantly in the primary chancre before treatment, but was unable to find any two or three days later. He aspirated fluid from the enlarged inguinal glands and found spirochetes constantly before treatment, but after three or four days after the injection of "606" they could not be found. More superficial lesions retrograded more rapidly. Primary scleroses and adenitis required the longest time, taking three or four weeks to disappear. The Wassermann reaction became negative usually between the twentieth and fortieth day after the injection, and in two cases on the eighth and tenth days. He noticed that the reaction became more intense immediately following the injection, and then gradually subsided. No untoward after-effects were observed.

The Treatment of Syphilis with Ehrlich's "606."—NICHOLS and FORDYCE (*Jour. Amer. Med. Assoc.*, 1910, lv, 1171) believe that we have in arsenobenzol a most thorough agent in controlling the manifestations of syphilis that are caused by the presence of treponema. They say that at present the method recommended by Wechsellmann seems to be the preferable one for administering the remedy. They call attention to the fact that delay or insufficiency in the amount of mercury in the early treatment of syphilis permits the entire system to become infected by *Treponema pallidum*, and damage to the bloodvessels or important structures takes place which might be prevented by energetic treatment. Although mercury and potassium iodide are efficient in the great majority of cases in controlling the manifestations of the disease, there are certain intractable cases in which they fail to control the symptoms, either on account of idiosyncrasy to one or both of these drugs or other causes. Furthermore, owing to the length of time required in treating a case of this infection patients often become discouraged and cease medication after a few months or a year or two. It is also well known that there are certain cutaneous and general manifestations of syphilis which respond slowly or not at all to mercury, even in heroic doses. Among these may be mentioned certain scaling syphilides of the palms, chronic nodular syphilides in patches of the type which clinically resembles lupus vulgaris, certain forms which affect the flush area of the face and bear a marked clinical resemblance to lupus erythematosus; also mucous membrane affections like leukoplakia, chronic interstitial glossitis, and relapsing deep and superficial lesions of the tongue and throat. Aside from these lesions which are under direct observation, there are the so-called parasyphilitic manifestations, such as tabes, the treatment of which by the classical drugs leaves much to be desired. In malignant syphilis with early destructive lesions and the development of profound cachexia, mercury, moreover, often fails to do good and not infrequently does harm. They conclude that it may reasonably be hoped that all the lesions which depend upon the presence of the organism will be favorably influenced, and the most we can expect in the secondary degenerative changes is that the process may become arrested. Further experiences with the drug will determine with more accuracy the dose which is necessary to bring

about a cure, the time that must elapse before a second dose can be safely given, and the more definite indications for its use after relapses or failure of a single dose to control the symptoms.

The Subcutaneous Use of "606."—MICHAELIS (*Berl. klin. Woch.*, 1910, xlvii, 1531) prefers the subcutaneous injection of this remedy, and says that he has found it well borne without exceptions. Often there was severe pain for some hours after the injection, but this was controlled by moist compresses. Sometimes a transient pain appeared again on the third day, but usually there was absolutely no sign of any inflammatory reaction. The great advantage presented by the subcutaneous method over the intramuscular injection is that walking and sitting are not interfered with by a dense infiltrate. The action of the remedy is more rapid than when it is given intramuscularly because of the greater surface exposed to resorption. Michaelis states that he has not seen any untoward by-effects in 71 cases of syphilis treated with Ehrlich's "606."

The Treatment of Sciatica with Epidural Injections.—BLUM (*Munch. med. Woch.*, 1910, lvii, 1681) refers by the term epidural injections to the anesthetization of the sacral nerve roots after they have left the cord, a method discovered simultaneously by Cathelin and Sècard. Blum has also used the perineural technique, and compares the two methods. He found that epidural injections were efficacious when the perineural injections failed. He injects from 5 to 10 c.c. into the spinal canal through the lower median sacral foramen, the needle piercing only the sacrococcygeal ligament. He says that the epidural method is not painful and has never caused fever or other untoward effects. On the other hand, injections by the perineural method have produced paralysis of the peroneus. Furthermore, epidural injections affect a wider nerve distribution than do perineural injections. Thus, the application of epidural injections is much wider, and they have been successfully used to relieve pain from compression of nerve roots by cancer of the spine, to relieve the gastric and bladder crises in tabes, and to relieve pain in lead colic. Furthermore, they have also been used for the treatment of nocturnal enuresis. Blum gives the details of the technique in his article which should be consulted in the original.

Chlorosis.—MORAWITZ (*Munch. med. Woch.*, 1910, lvii, 1425) forms the following conclusions as a result of his studies of chlorosis: (1) There are marked cases of chlorosis in which the condition of the blood is normal or nearly so. Such cases are not rare. The influence of iron is just as favorable in these cases as in those associated with distinct anemia. (2) Anemia is therefore not the cardinal symptom of chlorosis, but only one symptom among others. (3) The disturbances of menstruation, venous murmurs, and the majority of the subjective symptoms are not always dependent upon an anemia. (4) It is improbable that the curative action of iron in chlorosis is to be ascribed to a stimulative effect upon the formation of hemoglobin. The inferior action of iron in almost all non-chlorotic anemias, as compared with arsenic, aside from other observations, is an evidence against the existence of such a stimulative action. (5) Iron has a beneficial action in chlorosis not alone

because of its action upon the blood-forming organs, but also because of a direct action upon the, as yet unknown, cause of the disease. This, Morawitz suggests, may be a defective or excessive functioning of the ovaries or some interrelated ductless gland. The fact that chlorosis develops exclusively during puberty is also suggestive of this relation. He cites the observations of other men who have similar views, and gives the details of some cases he has observed. In these cases the percentage of hemoglobin was above 80 per cent. in nearly all, not below 60 per cent. in any, and frequently over 90 per cent. Morawitz does not believe that the mere loss and recovery of the difference between 80 and 90 per cent. of hemoglobin could either produce or cure the train of symptoms that make up the disease chlorosis.

The Present Status of Antityphoid Inoculation.—GOSMAN (*Jour. Amer. Med. Assoc.*, 1910, lv, 1169) gives a brief resume of the literature on inoculation for typhoid fever and the preparation of the vaccine and the methods of its use. In concluding, he says that it seems that the present status of these inoculations against typhoid fever is that they are valuable as a method of preventing the disease, and are, perhaps, the most valuable single asset we have in combating an epidemic, and that there is surely no doubt in the minds of most thinking and up-to-date medical men that they should be used in the following classes of persons: First, all nurses, ward attendants, hospital corps men, Red Cross assistants, physicians, and medical students; also all persons who contemplate a journey into a section where typhoid fever is known to exist or is suspected of existing. The inoculations should also be done generally in districts suffering from an epidemic, and especially in the families where a case exists; and in time of war all volunteers at camps of concentration should be inoculated as soon as possible after the camp is started. Gosman is convinced of the harmlessness and, at the same time, of the effectiveness of this procedure.

The Influence of Age and Temperature on the Potency of Antidiphtheritic Serum and Antitoxin Globulin Solution.—ANDERSON (*Jour. Infect. Dis.*, 1910, vii, 481) reports his work undertaken to determine the effect of age and temperature on the potency of diphtheria antitoxin. He tested both the untreated horse serum and the globulin preparation as made by the Gibson process. Each sample of serum was divided into three portions; one portion was kept at room temperature, one at 60° F., and the other at 40° F. The potency of each sample was determined every six months for three years. He found that the average yearly loss in potency of diphtheria antitoxin at room temperature was about 20 per cent.; at 60° F., about 10 per cent.; and at 40° F., about 6 per cent. He could determine little difference in the keeping properties of the untreated serum and the globulin preparations. He believes that if allowance is made for the decrease in potency, old serums are just as efficacious for therapeutic purposes as fresh serums. Diphtheria antitoxin to be placed upon the market and then kept under unknown conditions as regards temperature should be labelled with a return date not longer than ten years, and should contain an excess of at least 33 per cent. to allow for decrease in potency; in addition, when the serum is sold in syringes with an absorbable piston, an excess should be added for this loss. The only

disadvantage in using old serums would be the increased bulk of the injections for a given dose. Anderson also found that diphtheria antitoxin, if dried and kept in the dark at 40° F., retained its potency practically unimpaired for five and one-half years. He suggests that such a dried antitoxin might be of value on long voyages or in the tropics.

Deep Perineural Injections for the Relief of Neuralgia and Sciatica.—HECHT (*Med. Record*, 1910, lxxvii, 1040) reports his results in 60 cases of trifacial neuralgia. He used alcohol in ascending strengths of 70, 80, and 90 per cent. for the injections. Of the 60 patients, 37 were distinctly benefited (complete abeyance of pain for a longer or shorter period of time); 11 were improved (great reduction of pain); 8 were unimproved, and in 4 patients the pain was aggravated. Of the 37 patients benefited, 1 patient was entirely free from pain for one year and eight months. The shortest free interval from pain was two weeks. Hecht says this variability in results cannot be satisfactorily explained, but may be due to the accuracy with which the alcohol was deposited in, at, or near the nerve. With regard to the injection treatment of sciatica, Hecht says that alcohol injections are decidedly contraindicated. Harmful and even disastrous results have followed alcohol injections into mixed nerves. He reports a series of 33 cases of sciatica treated by the injection method. This method of treatment is limited to those cases in which the diagnosis of sciatica is made only after a rigid exclusion of all conditions that may give rise to sciatic pain as a symptom. Among the conditions that may give origin to pain similar to sciatica he mentions arthritis of the rheumatoid or deforming variety, tuberculous spondylitis, tabes, spinal syphilis, diabetes, inflammatory pelvic exudates, intermittent claudication, myalgia, and advanced general arteriosclerosis. He used deep intraneural injections of salt solution, and found that in most instances the relief from pain was almost immediate and complete. There were neither unpleasant effects nor any complications following the injections. Hecht also found that these injections benefited cases that may be classified from the site and distribution of the pain as myalgia.

The Action of Cod-liver Oil in Rachitis and Spasmodic Affections of Children.—ROSENSTERN (*Berlin. klin. Woch.*, 1910, xlvii, 822) reports his clinical experience that seems to confirm Schabad's conclusions with regard to the specific action of cod-liver oil upon the metabolism in rachitis and the convulsions so often associated with rachitis. Rosenstern gives the details of five cases of rachitis with marked craniotabes. In all these cases remarkable benefit followed the daily administration of 25 grams of cod-liver oil for three to six weeks. He thinks that phosphorus enhances the action of the cod-liver oil and advises the use of a mixture of 0.01 part of phosphorus to 250 parts of cod-liver oil. Of this mixture a teaspoonful is given five times a day to the severest cases. Cod-liver oil if given without phosphorus will have the same effect, but must be given in larger doses.

PEDIATRICS.

UNDER THE CHARGE OF

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The Diagnosis of Nasal Diphtheria in the Newborn and in Infants.—BLOCHMANN (*Berl. klin. Woch.*, 1910, xlvii, 2008) claims that nasal diphtheria in infants, in a large percentage of cases, is mistaken during the first days and even the first weeks of the disease for the ordinary "snuffles" or coryza. Notwithstanding the fact that this condition is frequent in infancy, and that the child's appearance is characteristic to the experienced eye, the true diagnosis is often not made until a rapid loss of weight and strength, a diphtheritic otitis media, or an absolute occlusion of the nasal passages make their appearance. It is, therefore, important to make a diagnosis immediately by direct nasal examination, before receiving the bacteriological report. It is desirable to be able to diagnosticate the bacilli carriers from those ill with the disease. Direct nasal inspection is remarkably easy in the newborn. In the recumbent position, with the child's nostrils separated by a bent hairpin or an open speculum, a good view of the nasal passages is obtained. If the child is not crying, pressing backward the tip of the nose is often sufficient. These methods were used in two epidemics among families. Three cases were diagnosticated as nasal diphtheria previous to a bacteriological report out of 8 cases of coryza. The second epidemic showed 5 infants, in their first week, infected by an adult. The first 2 cases showed coryza, and were diagnosticated diphtheritic by the direct nasal examination. This method then showed 3 other cases out of 16 children in the institution. These diagnoses were subsequently proved correct by cultures, and none of the remaining infants with coryza gave positive cultures or developed diphtheria. Among these 10 cases of nasal diphtheria, but 1 showed the characteristic discharge of bloody serum from the nostrils; 5 showed a thin membrane on the septum, which seems a rather frequent location. In only 1 case was the nasal floor involved. In a few cases the membrane involved the turbinates. The first epidemic developed in older infants, and was of the chronic type, almost always without fever. The membrane persisted in one case for over four weeks, and in another case the cultures were positive for three months. In the second epidemic 2 of the infants also developed diphtheritic inflammation of the navel, one dying of peritonitis. All the other cases recovered under antitoxin treatment. Only one child exhibited a rise in temperature. The foregoing history shows that rhinoscopic examination of the anterior fossæ is practicable in the newborn, and is an efficient method of preventing a dangerous neglect in diagnosis and delay in proper treatment.

Immunized Human Serum in Hereditary Syphilis.—MEIROWSKY and HARTMANN (*Medizinische Klinik*, 1910, vii, 1572) have investigated the effect of serum taken from syphilitics recently treated by "606" on the

lesions of hereditary syphilis in an infant. The good results obtained by treating nursing syphilitic mothers with "606," and influencing the child's condition through the mother's milk, led them to try the effect of the serum. The child of a syphilitic mother developed typical lesions of hereditary syphilis two weeks after birth. The lesions consisted of a pemphigus-like eruption on the soles of the feet, the palms and dorsum of the hands, and the buttocks. There were circumscribed areas of efflorescence around the mouth, on the ankles, and some around the buttocks. The mother's milk having failed, advantage was taken of the period to employ hypodermic injections of the human serum. The injections were as follows: September 3, 20 c.c.; September 6, 18 c.c.; September 7, 8 c.c.; September 9, 5 c.c.; September 10, 2 c.c.; September 11, 5 c.c.; September 14, 10 c.c.; September 16, 18 c.c. Two days after the first injection the soles of the feet were clear, the lesions on the hands much improved, and the efflorescence paling and showing a slight desquamation. The lesions continued to diminish, and on September 17 all the lesions had disappeared except a slight superficial desquamation at one place. Three days after the last injection there developed a periostitis of the right arm. Although not an entirely absolute cure, yet the efflorescence disappeared after the first injection, and the skin lesions which were progressive were halted and cured. The authors believe the effect of the injections would have been still more marked if they had had larger doses of the serum to use.

The Diagnosis of Epidemic Meningitis in Infants.—ERNST LEVY (*Medizinische Klinik*, 1910, vi, 1569) points out that the characteristic symptoms of acute onset, convulsions, and high fever, and the classical signs of rigidity of the neck and Kernig's sign do not usually appear in the meningitis of very young infants, excepting very late in the disease. Kernig's sign and rigidity of the neck are absent in from 50 per cent. to 60 per cent. of the cases under two years of age. Convulsions, which occur in so many infantile diseases, especially in spasmophilics, occur in young children with meningitis in only one-third of the cases. Intestinal irritation without fever and also inflammation of the entire respiratory tract often occur for weeks before some other definite symptom which indicates meningitis is found. Infants are especially liable to secondary infection of the lungs in meningitis, the true nature of which is thus often masked. With a few exceptions, almost all cases of meningitis in children of two years and under, Levy finds, have been treated for a variable length of time, even forty-five days, as cases of intestinal or pulmonary catarrh. Rigidity of the neck alone is a slight but fairly frequent accompaniment of these inflammations of the lung or intestine. A remittent type of fever is rather characteristic, the periods between the rises being short at first, and grow longer as the disease advances. There is often no febrile reaction at all. Levy has not found slowing of the pulse a characteristic feature, except in some forms of tuberculous meningitis. Symptoms referable to the central nervous system, such as the patellar reflex, etc., are, unfortunately, usually absent or doubtful. However, strabismus, usually fleeting, and pupillary inequalities are among the most constant signs of the disease. Hypersensitiveness, especially of the legs, is a cardinal symptom, as also are the pupillary dilatation from pain, on pinching the spine, and a reflex tremor of the

whole body or of a group of muscles on sitting the child erect or moving its limbs. This tremor, however, usually presents itself during or after the fourth week of the disease. Highly important from the diagnostic viewpoint are alterations in sight or hearing, such as blindness or deafness, following an illness of uncertain nature. Subsequent to such an illness, otitis media, neuroretinitis, or iridochoroiditis invariably means meningitis. In infants, a widening of the fontanelles is of great diagnostic value, as showing increased tension of the cerebral fluid. This is often an early sign and a common condition in epidemic meningitis. Ventricular puncture is important in diagnosing all cases showing increased tension of the cerebral fluid, as the cocci are often found here when they are absent in the spinal fluid. Lumbar puncture is essential; but as this means is not always available, and a bacteriological examination requires time, a provisional diagnosis at least should be made from the symptom complex, so that treatment by serum injection may not be delayed.

An Epidemic of Anterior Poliomyelitis in Austria.—GEORG STIEFLER (*Medizinische Klinik*, 1910, vi, 1743) reviews the history of anterior poliomyelitis in Europe, America, and Australia, and notes the different aspects in symptomatology, after-effects, and mortality shown by different epidemics. The clinical picture constantly changes in the different epidemics. In some, gastro-enteric symptoms predominate, in others they are absent. Some epidemics show apparently all forms—abortive, intestinal, spinal, bulbar, meningitic, etc. Mortalities range from 10 per cent. to 22 per cent. The constant and characteristic symptom in all of them is the paralysis with the acute degenerative changes in the central nervous system. Distribution of the epidemics among the summer and fall months is constant. A consensus of opinion has developed that the disease is infectious. That it is spread by contact with infected individuals seems highly probable. That it can be carried by a third, healthy person is doubtful at present writing. Stiefler particularly reports the epidemic in northern Austria in 1909. Most of the thickly settled and industrial communities escaped the disease. Most of the cases occurred among small landowners and laborers, but numbers of the well-to-do also were affected. The greatest number of cases occurred in children aged from one to three years. A relatively high proportion occurred in children aged from six to fourteen years, and 15 per cent. occurred in adults. The disease was prevalent from August to January, with the largest number of cases in October. The clinical aspect showed usually a rather short prodromal stage with variable symptoms. Besides the usual prostration, anorexia, pain in the head, neck, back, and limbs, there was frequently seen an angina and a respiratory catarrh. Gastro-intestinal symptoms, such as nausea, vomiting, constipation, or, less frequently, diarrhoea, were often seen. The paralysis was always of the atrophic, degenerative type, reaching its maximum within a few days, then receding and persisting only in certain groups of muscles. The meningitic type rarely appeared, and only twice were the bladder and rectum involved. Pain was present in most cases; sometimes it was general, sometimes limited to the paralyzed muscles. Tenderness on pressure was common in the muscles and nerve trunks. The fever was moderate throughout, and lasted but a

few days. The abortive type was rare. Complete recovery occurred in 22 per cent. of the cases. Most of the other cases recovered with physical defects. The mortality was 12.99 per cent. The pathological process is not always limited to the anterior horns, but may affect the posterior horns and the gray matter of the brain or cord. The disease attacked two or more members of the same family in seven instances, the second case appearing from two to twelve days after the first case developed. In a number of cases the disease showed a decidedly contagious character.

OBSTETRICS.

UNDER THE CHARGE OF

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Pernicious Nausea of Pregnancy Treated by Thyroidin.—SIEGMUND (*Zentralbl. f. Gynäk.*, 1910, No. 42) reports 5 cases of pernicious nausea of pregnancy, in which he has had good results by the administration of thyroidin. Four of these cases were under his immediate observation, and one was treated by a colleague. The remedy is administered several hours before the time when the worst paroxysms of vomiting appear. The stomach must be absolutely empty at the time of the administration. It is usually best to give it in the early morning before the patient leaves her bed. She is encouraged to sleep afterward and to take nourishment before getting up. From an hour to half an hour, however, before the other meals of the day, the remedy should be used, and also before going to bed. The morning dose should be the largest, 6 decigrams being given in some cases. If the patient vomits in the evening, a similar dose should be given before this time. The remedy is best used in powder, and sometimes sodium bicarbonate or bismuth may be combined with it to advantage. In other cases, fresh glycerin extract of the gland is used to advantage. In most severe cases Merck's preparation for hypodermic injection may be administered with prompt results. If the vomiting can be controlled the patient should be fed with small quantities of easily digested food, usually liquid. Meat should be avoided. An examination of the urine of these patients showed no disturbance from the remedy, and no bad symptoms developed during its use. Bossi's experiments of giving such cases suprarenal extract was also tried by the author, and in some cases with apparently good results. It has also been observed that in some patients in which the secretion of milk is deficient, the administration of thyroid extract is of decided value.

The Tetany of Pregnancy.—FRANK (*Monatss. f. Geburt. u. Gynäk.*, 1910, xxxii, Heft 4) reports 5 cases of tetany complicating pregnancy. They presented the usual symptoms of muscular cramp in anemic and depleted patients. The fifth case was especially interesting and

typical. The patient was pregnant for the sixteenth time. She had given birth to twelve children, who had died, three remaining alive. In her last pregnancy she had central placenta prævia, and was delivered by version and extraction, with severe hemorrhage. For two months she had had cramps in the hands and in the muscles of the face, which were exceedingly painful, and were not relieved by medication. Recently these cramps became almost continuous. On admission to the hospital the uterus was two fingers' breadth above the umbilicus, and the patient's muscular cramps extended to the upper and lower extremities, and occasionally to the muscles of respiration. When this happened the patient became partially unconscious. The cramps were so severe that full doses of chloral, bromide, and morphine, were given with but very little relief. Labor was induced, after which the patient was considerably better for a time. In the sixth day of the puerperal period she was suddenly taken with fever and a return of the convulsions. This gradually subsided, and the patient made a good recovery. In discussing the causation of the disease, it seems to be a toxemia occasioned by the failure of the immunizing substances in the body to neutralize the toxin produced in the placenta. Others think that the patient produces in her own body so great an amount of toxin that the epithelia of the body cannot neutralize it. In most cases the disease returns in succeeding pregnancies, while the patient is absolutely free when not in the pregnant condition. Multiparæ are most often attacked, and, as a rule, only nervous and anemic primiparæ. The symptoms are most pronounced in the latter half of pregnancy. In each succeeding pregnancy the disease is worse, the cramps gradually attacking not only the upper extremities, but the various groups of muscles throughout the body. Rapidly succeeding pregnancy makes the disease especially severe. The occurrence of hemorrhage in a previous pregnancy predisposes to the disease in the next pregnancy. Meinert reports the case of a patient from whom a goitre was removed in the fourth month of gestation; three days after operation she had tetany, which disappeared in two weeks. The labor was normal. A year later the patient again became pregnant, when tetany returned with such severity that it was necessary to interrupt the pregnancy. As a rule, the cases proceed to recovery. Many mild cases do not come to the attention of a physician. The treatment consists, in mild cases, in rest, forced nutrition, and the use of bromides. In severe cases the pregnancy must often be interrupted when tetany follows extirpation of the thyroid gland. Schauta, who has seen large numbers of these cases, does not believe that when the thyroid gland has not been removed tetany is sufficient reason for inducing labor.

Combined External and Vaginal Version.—STOWE (*Amer. Jour. Obst.*, October, 1910) reports 13 cases of combined external and vaginal version. His experience with these leads him to conclude that combined external and vaginal version is not dependent upon the size of the cervix nor the degree of its effacement. The less the cervix is dilated the more easy the operation, if the membranes are unruptured. During the latter weeks of pregnancy it is often impossible to correct a malpresentation by external methods only. A preliminary dilatation of the perineum in primiparæ, and the performance of this combined

version, does not tend to interrupt pregnancy. In none of these cases did the foetus, when turned resume its abnormal position. No evidence of separation of the placenta was observed, and in no case were the heart-sounds of the child altered. The proper presentation of the foetus by the cortex or breech, should be obtained by this method. The operator may choose in accordance with the conditions present. Should amniotic liquid escape during the first stage, version should be done as soon as possible. The danger of separation of the placenta depends upon the degree of uterine contraction and the amount of amniotic liquid present. If the hand does not enter the uterus septic infection rarely occurs. In some cases of placenta prævia the foot can be brought down to the inlet before the membranes are ruptured. This is easier than the classic Braxton-Hicks method.

The Treatment of Fibroids Complicating Pregnancy.—TATE (*Brit. Med. Jour.*, October 22, 1910) draws attention to the unfavorable changes which may occur in fibroids during pregnancy. He believes that should a patient having a very large fibroid become pregnant, serious symptoms may develop in the latter half of pregnancy from upward pressure on the diaphragm caused by the rapid increase in the size of the uterus. Necrosis in the tumor may cause discomfort or persistent pain and make interference with the pregnancy necessary. Torsion of the pedicle in a fibroid tumor is so rare that it need not be regarded as a practical danger. Small fibroids above the brim of the pelvis do not, as a rule, undergo important changes during pregnancy. It is estimated that from 20 to 25 per cent. of women having fibroids abort because of the presence of the tumor. Retention of a portion of placenta and septic infection are not uncommon in these cases, and may necessitate hysterectomy. During labor a fibroid tumor may become wedged in the pelvis, making vaginal delivery impossible. This accident should have been anticipated if the patient is seen in pregnancy and examined, when it is usually possible to dislodge the tumor into the abdomen before labor begins. Occasionally a fibroid uterus may rupture during labor because the uterine wall has become thinned over the tumor. Cases in which hysterectomy is imperative during labor are not very common, and this operation may usually be made elective by an examination of such patients during pregnancy. During the puerperal period postpartum hemorrhage must be anticipated and treated. It may be difficult to control this, because the tumor may become partially dislodged from its bed and great difficulty be found in controlling the discharge of blood from the uterine sinuses. Fibroid tumors may also become detached and partially extruded during the puerperal period; and if sloughing occurs the patient is exposed to the danger of septic infection. When fibroids are situated in the pelvis, and must necessarily obstruct labor, if the tumor is mobile it is usually possible under anesthesia to push it above the pelvic brim and allow the pregnancy to go on. If the tumor is firmly impacted in the pelvis, it is safer to perform abdominal section, with the hope of enucleating the tumor from the uterine wall. Small fibroid polyps attached to the cervix should be let alone if possible, as interference tends to bring on abortion and hemorrhage. When fibroids are multiple and encroach upon the lower uterine segment, it is impossible to

predict with certainty the behavior of the tumor during labor. Such tumors often change their position during parturition, rising gradually into the abdomen as the child descends. When fibroids are entirely abdominal tumors, severe symptoms are rare and operative interference is seldom necessary. The greater number can be treated by myomectomy successfully. Interstitial fibroids rarely justify interference during pregnancy, and should operation be done it is usually best to remove the uterus. If possible, an operation should be deferred until full term, and even then myomectomy may be selected, if possible. The induction of abortion or premature labor should not be undertaken in cases complicated by fibroids because the risk of hemorrhage and septic infection are too great. In view of the fact that many of these patients have but one pregnancy, it is well to take every conservative measure to bring that pregnancy to a successful termination.

Lockyer (*Ibid.*) reports in detail 9 cases of fibroid tumors of the uterus complicating pregnancy. In 3 of these the tumor was incarcerated in the pelvis; in 4 of them operation was performed, followed by uninterrupted recovery; in 3 the uterus was removed; and in 1 the tumor was removed and also a right-sided ovarian cyst. This patient's pregnancy was not interrupted and she had a spontaneous delivery afterward. In 5 cases operation was not done, as the tumor was not in a position to become incarcerated or to be dislodged under anesthesia. In 1 of the cases abortion occurred, and difficulty was experienced in removing the placenta.

GYNECOLOGY.

UNDER THE CHARGE OF
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An Improved and Perfected Operation for the Relief of Extreme Cases of Procidentia, Cystocele, and Rectocele.—Goffe (*Amer. Jour. of Obstet.*, 1910, lxii, 611) claims that when the uterus and bladder are in their normal position the pelvic floor exercises no influence whatever in their support, which is obtained only by the suspension of their ligaments to the bony framework. The association of prolapse and relaxation of the outlet is due not to the loss of the support as afforded by the perineum, but to the introduction of a new force—the rectocele—which exerts traction on the cervix to which the ligamentous attachments must eventually succumb, permitting the uterus to assume the varying degrees of prolapse. The reason for absence of prolapse in complete tear is that no pull is exerted on the cervix. Repair of the perineum is essential to the treatment of these conditions in order to eliminate the drag of the rectocele. The bladder is likewise held in position by suspension. One support is the uterus, to which the bladder and upper end of the vagina are intimately attached; a second support is afforded by the fascia lata, which, coming under the bladder from its lateral insertion,

acts like a sling. Cystocele, therefore, is due to a descent of the upper support of the bladder—the uterus—and the yielding of the vaginal sheath, permitting a hernia of the bladder. An additional factor is sliding of the various planes of tissue composing the vesicovaginal septum. Based upon these conceptions of production, the author has devised operative procedures to meet the conditions presented. Briefly summarized, the operation for cystocele consists, first, in a free dissection of the bladder from its attachments. After suspending the uterus by shortening the ligaments, the bladder is restored to its normal position and held in place by three catgut sutures, one at its fundus and one at each cornu, thus spreading out and fixing the base of the bladder. After excising the excess of tissue, the fascial sheath and vaginal mucosa are sutured. In case of extreme procidentia, a vaginal hysterectomy is performed and the broad ligaments are sutured together across the pelvis, taking up all slack necessary to make them taut. Upon this support the bladder is spread and sutured, as previously mentioned. The upper end of the vagina is also attached to the broad ligaments after removing sufficient tissue to obtain the support of the fascia lata. In all cases in which a rectocele exists the perineum is repaired.

The Radical Cure of Hemorrhoids: Modified Whitehead's Operation.—By omitting dilatation of the sphincter, O'CONOR (*Lancet*, 1910, clxxix, 946) has found that the operation for hemorrhoids can be easily performed in a short time with but little loss of blood. He emphasizes the importance of removing only the thin cuff of mucous membrane along with the loose areolar tissue which bears the hemorrhoidal veins, of carefully avoiding injury to the sphincter by using the senses of sight and touch, and not encroaching too much on the skin when making the primary circular incision. Four Lane's forceps are applied to the four cardinal points of the anal circle exactly at the mucocutaneous junction, irrespective of rugosities. With scissors each segment is divided at the mucodermal line until the circumference has been completed, the primary cut including skin and some subcutaneous tissue. The left index finger is inserted into the anal canal and the separation carried down to the submucosa; the external sphincter is pushed upward with a blunt dissector. No further advance must be made until the submucosa is well defined throughout the whole circumference, and the sphincter has been freed. During the process of freeing the mucosa, forceps are applied to its cut edge to serve as tractors. By blunt dissection the cuff is freed as high as the internal sphincter, which is indicated by the transverse fold of mucous membrane. A vertical slit is made in the mucosa up to this point and the apex sutured to the skin; the cuff is excised by a series of transverse cuts, uniting the mucosa and skin with a continuous catgut suture as the division progresses. Fibrous strictures resulted in 2 out of 450 cases thus treated; a partial recurrence occurred in one patient, who subsequently developed cirrhosis of the liver.

The Wertherim-Schauta Operation.—Based upon his experience in 40 cases, STOECKEL (*Archiv f. Gynäk.*, 1910, xci, 546) details the important points in operative technique as well as a few of the complications which he has observed during convalescence. The operation is used in cases

of cystocele, and consists in the interposition of the uterus between the base of the bladder and the anterior vaginal wall. Of great importance is complete mobilization of the cystocele sack. Too frequently the bladder is separated from the anterior cervical wall only sufficiently to permit delivery of the uterus through the uterovesical fold of peritoneum, which produces an elevation of the centre of the cystocele, leaving unaltered a pouch on either side. Total recurrence is certain to follow, due to the constant traction exerted by these lateral recesses. Complete mobilization of the cystocele requires division of the so-called "bladder pillars," which consist of dense tissue extending from the base of the bladder to the anterior vaginal wall. To avoid hemorrhage, these ligaments should be divided between ligatures. Injury to the ureters will be obviated by incising the pillars transversely close to the vaginal wall at the lower angle of the colporrhaphy wound. Secondly, the uterus must be placed in such a position that it supports the whole bladder. Every uterus which is brought in the position of forced anteversion has the tendency to upright itself. Should this tendency be marked, the fundus will project into the bladder, leaving unsupported a portion anterior to it; or there may be a complete or partial separation of the uterus from its points of fixation. Should force be necessary to bring the uterus under the urethra, the interposition is contraindicated. When the uterus is too small to serve as a proper support, a broad base is obtained by suturing the round ligaments to the vaginal wall. Enlargement of the uterus due to chronic metritis is especially adaptable for this purpose. The cervix is amputated only when it forms a sharp angle with the body of the uterus. In every case the uterine cavity is examined by incising the anterior wall from the fundus to the internal os; after thorough cauterization, this incision is closed. As the last important point, Stoeckel urges that complete hemostasis be secured. Bladder symptoms of varying intensity frequently follow the operation. In one case dribbling of urine developed a few weeks after operation, due to a sacculation of the bladder immediately posterior to the urethra, which resulted from spontaneous elevation of the uterus; a second case, in which the bladder was accidentally opened, developed a stubborn cystitis, which was aggravated by the distortion of the bladder incident to operation. One death resulted from pulmonary embolism. The only disadvantages to this operation are the length of time necessary for its performance, and the increased disposition to thrombosis. Especial care is advisable in the presence of a demonstrable myocarditis.

The Structure of the Stroma of the Endometrium and its Bearing on the Menstrual Changes.—As the result of his studies, YOUNG (*Brit. Med. Jour.*, 1910, ii, 1214) states the following conclusions: The stroma of the endometrium consists of a soft semifluid protoplasmic mass, imperfectly differentiated into cellular elements. The cells anastomose freely with one another by means of protoplasmic processes. They present many and varying alterations in shape, but these are easily dispelled, and the cells then approximate to the typical stellate shape. The differentiation of the stroma cells is thus probably more apparent than real. The intercellular spaces, in all probability, do not directly communicate with one another. The anastomosing processes

are not, as is usually stated, filaments, but films of protoplasm, which under ordinary circumstances close in the fluid cavities. The intima and media of the vessels are nothing more than ordinary flattened stroma cells. This shape they easily lose. Except in the deepest layers of the mucosa, the vessels have no specialized supporting coats (muscle, elastic tissue). The vessels are obviously so constructed as to allow a ready and universal opening up of their walls, and the structure and consistence of the stroma such as to permit its ready displacement by fluid or blood. The œdematous infiltration of the tissues, which precedes the hemorrhagic escape, is due neither to a mechanical displacement or filtration of fluid from the vessels, nor to a secretory activity of the intimal cells. It is dependent on protoplasmic changes, which result in an active imbibition of fluid from the vessels by a process of osmosis. So far as we at present know, this change is due to a widespread liberation of crystalloid elements in the tissues. The infiltration of the stroma with blood corpuscles is, in all probability, due to exactly the same cause. In consequence of its peculiar structure, the uterine mucosa must be looked upon, throughout its whole extent, as a potential blood sponge.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Self-inflicted Ocular Traumatism among Russian Conscripts.—SEIDENMANN (*Centralbl. f. prak. Augenhk.*, October, 1910, p. 293) finds that such injuries, usually involving the right eye, and either self-inflicted or betraying the unskilled handiwork of the quack, may be comprised under three categories: (a) Opacities of the cornea opposite the pupil; (b) traumatic cataracts; and (c) destruction of the entire globe through application of leeches to the cornea. The mechanism producing the corneal injuries is not entirely certain. It is probable that that membrane is first cauterized with nitrate of silver and the wound thus caused treated with potassium iodide. The cataracts always betray their origin by the minute corneal opacities which gave entrance to the needle. The leeches, the cruellest method of all, suck out the aqueous humor, causing extensive intra-ocular hemorrhage, with detachment of the retina and choroid. The final result is a shrunken stump.

Pigmentation of the Retina in Nephritis.—RACHLIS (*Klin. Monatsbl. f. Augenhk.*, September, 1910, p. 322) from microscopic examination. concludes that pigmentation of the retina in nephritis may occur from degenerative changes of the external and middle layers of that

membrane, the choriocapillaris being intact. Such degenerative changes of the retina can be regarded as consequences of the nephritis. They are not analagous to the pigmentation which occurs in the fatty cells in fatty infiltration of the retina. The ophthalmoscopic appearances of choroiditis disseminata are sometimes found in changes of the pigment epithelium and retina alone when the choroid itself is healthy.

Isolated Monolateral Paralysis of the Third Nerve of Aneurysmal Origin.—From an analysis of cases of this kind, including a personal observation, PASCHEFF (*Archiv. d'ophtal.*, October, 1910, p. 634) finds that when an aneurysm causes paralysis of the third nerve alone, it is uniformly seated upon the trunk of the internal carotid, between the origins of the anterior and posterior communicating arterics. When the aneurysm involves the origin of the posterior cerebral artery, the paralysis of the third nerve is accompanied by paralysis of the corresponding facial. The only subjective symptoms (besides the diplopia) are pains in the head and constant noises upon the same side as the aneurysm. These cases always end fatally, usually quite suddenly, shortly after the appearance of the paralysis.

Detachment of the Retina Treated by Tuberculin.—Poorly or non-vascularized tissues like the tendons, aponeuroses, serous membranes, cartilage, being the seats of election of bacillary lesions, DOR (*Clin. ophtal.*, August, 10, 1910, p. 362) raises the question whether the vitreous body might not be added to the same list. Detachment of the retina, being secondary to retraction of the vitreous, presupposes antecedent disease of that body. The fact that the lesion is particularly apt to occur in myopia argues that the latter simply creates the anatomical conditions favorable to such an occurrence, just as osseous tuberculosis affects by preference bones which have undergone too rapid growth. Upon systematically questioning patients suffering from detachment, he has frequently found an antecedent pleurisy, arthritis, adenopathy, chronic rheumatism, or chronic bronchitis. Based upon such considerations, he has treated five cases of detachment by tuberculin, with complete and permanent re-application of the retina in three cases, re-application followed by relapse in one, and failure in a fifth—a degree of success which can certainly not be the result of coincidence.

The Principal Meridians in Astigmatism in Relation to the Lateral Inclination of the Head.—ORESTE (*Ann. d'ocul.*, June, 1910, p. 459) has studied the changes in the direction of the principal meridians in astigmatism when the head is inclined laterally. He finds that in the majority of cases the eye executes a movement of rotation about its antero-posterior axis in the inverse direction, to compensate, in part, the lateral inclination of the head. This movement of compensatory rotation, nil in some cases, varies in general between one and four to five degrees on the average, but may attain as much as eight. In some cases such compensation takes place in a single direction only. It has been supposed that when a vertical line is fixed, and the head is thence turned laterally, the line continues to be seen in its vertical position because the eye tends to return to the primitive position. The compensation possible, however, is too weak to overcome inclination of the head of any considerable

amount. Hence the correct vision of vertical lines under these circumstances is a phenomenon of psychic origin due to the fact that the subject is conscious of the position of his eyes, and makes the requisite allowances.

Unilateral Cataract from Electricity.—BICHELONNE (*Annal. d'oculist.*, August, 1910, p. 108) concludes that, considering the number of instances of accidental contact with currents of high power, cataract from such a cause is rare, a circumstance which may be due to the fact that the crystalline lens becomes affected only when one of the points of contact is not far from the eye itself, which is also a rare occurrence, for the contact is most commonly made by the two hands. For the same reason the cataract is almost always localized upon the affected side. Voltage seems to have little influence. The opacity of the lens is tardy in appearing, and seems to be dependent not upon lesions of the nerve centres or peripheral nerves, but upon a local trophic disturbance, circulatory or otherwise, which manifests itself upon an organ more vulnerable than the neighboring parts.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Interrelation of Glands of Internal Secretion. III. Chemotaxis.—BERTELLI, FALTA, and SCHWEEGER (*Ztschr. f. klin. Med.*, 1910, lxxi, 23) have studied the effect which a number of substances show upon the cells of the circulating blood when injected subcutaneously into dogs. These substances were adrenalin, pilocarpine, atropine, sodium nitrite, extracts of the infundibular and glandular portions of the pituitary body, cholein hydrochlorate, and ergotin. They find that, in general, these substances may be divided into two groups according to their effects upon the blood cells, or rather upon the blood-forming organs. The first group, represented by adrenalin and atropine, produces a rapid, marked, and prolonged hyperleukocytosis, accompanied at first by increase in the eosinophilic cells and later by disappearance of these cells from the blood. Adrenalin, moreover, gives rise to a rapid polycythemia, for the red cells increased ten minutes after injection 40 per cent. and after five hours at times 70 to 100 per cent. The second group includes all the other substances, and their action is characterized by the following effects: At first there is transitory accumulation of the neutrophilic leukocytes in the internal organs, and especially in the liver, while at the same time there is an actual increase in the mononuclear cells in the peripheral circulation and more or less pronounced hyper eosinophilia. Later, the blood shows an increase in the neutrophilic and eosinophilic leukocytes. The action of adrenalin and of the substances in the second group is not believed to be dependent upon

blood pressure changes nor upon changes in the caliber of the capillaries, nor does the explanation based by Ehrlich upon the theory of negative and positive chemotaxis seem adequate to explain the action of these substances. The authors point out the fact that the substances in each of the two groups have in common a similar action on the nervous system: adrenalin, for instance, acting as an excitant to sympathetic nerves. This analogy is suggestive in connection with the prompt response of the cells of the blood to injections of adrenalin, and there is good reason to suppose that the substances in the first group act as stimulators of the bone marrow and of increased blood formation. The explanation for local chemotaxis is not clear, but it seems at least that when substances arrive in the circulation the chemotactic stimulus runs parallel with the variation in tone of the sympathetic nervous system. The authors suggest that the variations in the output of cells from the blood-forming organs may be in part controlled by internal secretions.

The Venous Pulse in Fibrillation of the Auricle in the Mammalian Heart, with Reference to the Venous Pulse in Pulsus Irregularis Perpetuus.—RIHL (*Ztschr. f. exp. Path. u. Therap.*, 1910, vii, 693) has studied the graphic tracings made by means of a special tambour from the jugular veins in dogs in which fibrillation of the auricle was produced by electrical stimulation of the vagus nerve. The carotid and subclavian arteries on the side from which the venous tracings were made were tied off to prevent a transmitted pulsation to the vein. The activity of the auricle and ventricle was recorded by the suspension method. Since the method of tracing the waves in the jugular vein was the same as that employed in man, the venous tracings were comparable to those taken from human subjects. Before the production of fibrillation of the auricle the venous pulse showed a well-marked *a* wave, followed by the two waves of ventricular origin. After the establishment of fibrillation of the auricle the *a* wave disappeared entirely from the venous tracings, leaving only the two waves of ventricular origin. The tracings therefore corresponded exactly with those which are obtained in man in pulsus irregularis perpetuus, not only in the disappearance in the wave produced by the contraction of the auricle, but even in certain minute details concerning the size and variation in the waves dependent upon the ventricular action.

The Keith-Flack Node in the Production of Cardiac Arrhythmia.—The recent investigations of Walter Koeh upon the anatomy and pathology of the bundle of muscle described originally by Keith and Flack as lying between the vena cava superior and the auricle, has suggested that certain pathological changes in this region may possibly play a part in the production of some of the cardiac diseases which at the present are not perfectly understood. Thorel, too, has described a bundle of muscle fibers which connects the sinus node with the node of Tawara in the auricle. Owing to the probable interest which the Keith-Flack node may have for clinical medicine, MacKenzie already having suggested that lesions of this muscle bundle may be connected with perpetual arrhythmia, JAGER (*Deut. Arch. f. klin. Med.*, 1910, c, 1) has destroyed the node in 15 dogs and 45 cats in order to see what effect

this might have upon the rhythm of the heart. The node was destroyed by a hot instrument, serial sections being made later to determine whether the entire muscle bundle was destroyed. The experiments were successful in 8 cats and 6 dogs, but total destruction of the Keith-Flack node failed to give rise to any arrhythmia of the heart. Jäger therefore concludes that the results obtained by Hering after cutting the venoauricular junction, namely, cessation of the beat of the auricle, was not due to injury to the node, and that such injuries do not give rise in dogs and cats at least to a disturbance in rhythm of the heart.

The Substitution of Strontium for Calcium in Bones.—LEHNERDT (*Ziegler's Beiträge*, 1909, xlvii, 468; 1910, xlvii, 213) in a series of interesting experiments has fed pregnant rabbits strontium phosphate. Usually calcium was eliminated from the diet, but in a few experiments strontium phosphate was simply added to the animal's ordinary food. He has found that by this means profound changes are brought about in the bones of the young of the pregnant rabbits. These consist in deformities, principally of the long bones, and resemble to a certain extent the pathological lesions of rickets. They are, however, not exactly the same, and should be termed pseudorickets. The action of strontium is that of a formative stimulus to the bones, and the absorption of large quantities of this salt by the foetus in the absence of calcium gives rise to spongy osteoid formations at the ends of the bones, with rapid union and great decrease in the absorption of bone. When calcium is fed in small amounts together with strontium, the spongy outgrowths show some calcification, but with an increase in the amount of calcium the abnormal changes in the bone diminish. In a second communication Lehnerdt describes some further experiments carried out under the same conditions with newborn puppies. The results here were much the same as in the first series of experiments, and the changes occurring in the bones were those of a pseudorickets, consisting in diminished resorption of bone with exaggerated apposition in bones which were of normal length. When fractures occurred they healed with the formation of an excess of callous; when calcium was added to the food the spongy osteoid growths became calcified. The action of strontium appears in many ways like that of phosphorus, though there are certain differences in the effects of the two drugs. Lehnerdt finally suggests that strontium may be of therapeutic value in osteomalacia, in such conditions as osteoporosis when there is an increased resorption of bone, and in conditions in which callous formation is delayed and slight.

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THE
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ORIGINAL ARTICLES.

THE MEDICINAL TREATMENT OF DIABETES MELLITUS.

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It may be freely admitted that the progress in the treatment of diabetes mellitus has been due to the more or less scientific appreciation of dietetics, which leads to the reduction or removal of the sugar in the urine. Although there is no scientific explanation why certain carbohydrates, such as are found in oatmeal, in potatoes, even in glucose itself, may not only do no harm, but do good, yet the dietetic treatment for the present, and possibly for some time to come, is the one which should be instituted in every case whenever possible. At all events, and this always is the essential in every therapeutic procedure, in our present state of knowledge, it leads to the best results in the greatest number of cases. Moreover, most experts are united in saying "that without suitable diet a favorable influence upon the disease is excluded" (Naunyn). But when we come to the final analysis of the effects of this mode of treatment, they are only of a symptomatic nature—followed, it is true, in individual cases by more or less lasting improvement. It may also be admitted that in rare cases this treatment leads to a cure of the disease, as occurs in other diseases in which the cause of the disease is removed by removing the symptoms produced by it. That the prevention of certain not infrequently fatal complications may be accomplished by dietetic treatment is an established fact.

The question whether all this can be accomplished in any other way should also seriously engage our attention. Indeed, there comes up, first, a question of much greater importance: Is there any-

thing by which the cause of the disease can be removed? In order to do this, and as dieting is only rarely causal, some other remedy should be found. The problem, then, is first to find a causal procedure; and second, if this cannot be done, some symptomatic treatment which can be applied in every case with benefit. The dietetic treatment fails for two reasons: First, because it is of little or no value, that is, the urine cannot be made sugar-free by it, or its sugar cannot be sufficiently reduced; and second, because it is impossible to have dieting carried out by the patient. Notwithstanding all efforts to impress upon him the absolute necessity of dieting, the advice is not heeded in a certain percentage of private patients (15 to 20 per cent. in my experience). Moreover, there is a large number of patients who cannot, for external reasons, pursue this treatment. In these circumstances it is natural that medicine should be tried. It is from the two kinds of patients just described that my conclusions are drawn.

Before the present era medicine was prescribed in every case of diabetes mellitus; the medical pendulum then swung to the other extreme, and now medicine is rarely given. In most instances the drugs were prescribed in a purely empirical way—recommended by some great clinical master; they were employed by those within the circle of his influence. At other times, remedies were applied on account of some physiological discovery, as the employment of arsenic, which prevents the development of glycosuria when Claude Bernard's piqure is done. More frequently, however, some remedy was given which gave symptomatic relief, more or less temporary, and, in its turn, was discarded when some newer drug was recommended. Some idea of the number of drugs recommended can be obtained from the statement that in the fifth edition of the *National Dispensatory* (1894) forty-two remedies are given, to which there may be added forty-five more up to the present time, without making the list a complete one. It is not astounding, therefore, that skepticism as to the value of medicinal treatment controls the present therapeutic situation. So much so is this the case that Stadelmann claims that no medicine does good in diabetes mellitus. This has not been the case in my experience, as will be shown later.

The action of drugs may be a causal one, as has been intimated before, since the general condition of the patient or the disease which is at the bottom of the diabetes (the liver, circulatory apparatus, the nervous system) may be favorably affected: this from Naunyn,¹ who says that, opium excepted, he considers the internal remedies which have been recommended are "variable, unreliable, or ineffectual." Notwithstanding the latter statement, which especially applies to antidiabetica, there is a large field open for causal treatment—that of arteriosclerosis, the cirrhosis of the liver, including

the liver in chronic cholangitis, from whatever cause, and chronic myocardial insufficiency.

Since von Mering and Minkowski² established a relation between the pancreas and diabetes mellitus, pancreatic preparations have been prescribed. Given with all precaution, these preparations have failed to produce any effects in the cases in which I have tried them. The same preparations which had been tested by artificial digestion and followed by good results when given for digestive troubles, failed entirely in diabetes mellitus. This is readily explained by the fact that pancreatic failure is frequently not the primary cause of the disease, but the expression of faulty internal secretion, involving, as we know, at least three glands, and possibly more.

Funck³ has again called attention to the condition of the gastro-intestinal tract for causal treatment. He has reported six cases which were treated by considering gastro-intestinal disease as the cause of the diabetes. The diet prescribed was that indicated for the alimentary trouble, and in the individual case carbohydrate metabolism in its relation to diabetes was entirely disregarded. By this mode of treatment his patients were cured in the sense that they could be put upon a diet of 3000 calories for three days, largely consisting of carbohydrates, and remain sugar-free. Sawyer, of Cleveland, has for quite a number of years employed lavage of the stomach and appropriate diet. He reported⁴ 19 cases in 1905, in all of which amelioration of symptoms followed lavage of the stomach, and in some a clinical cure. He states that "the most striking influence has been observed on the polyuria and thirst." Although the percentage of sugar may not be reduced, the diminution in the quantity of urine is followed by a diminished loss of sugar and, therefore, a corresponding gain to the patient. Strübe has done the same.

Diseases of the nervous system should also be considered for causal therapy; a glance at the list of nervous diseases which are said to produce diabetes mellitus will show how much can be expected from causal treatment under these circumstances. In the brain there are syphilis (*vide infra*), apoplexy, acute brain softening, paresis, injuries of various kinds; in the spinal cord, tumors, myelitis, multiple sclerosis, locomotor ataxia, various lesions in the peripheral and the sympathetic nerves, and the various neuroses. Syphilis occurs very often with diabetes mellitus, and it is accused of producing this disease either by a local lesion or in some intangible manner, as it occurs in so many other diseases—all of which is by way of being cleared up at the present day. At the time of writing, and purely as the result of clinical experience, it must be confessed that the ordinary antisiphilitic treatment does not have much effect upon

² Archiv f. exper. Path. u. Pharm., 1907, xxvi.

³ Münch. med. Woch., 1910, p. 1224.

⁴ Trans. Assoc. Amer. Phys., 1905, xx, 446.

diabetes mellitus. In my whole experience I have not seen a single case in which any therapeutic effect was produced upon diabetes mellitus by mercury or iodides, so that my indication for antisyphilitic treatment in these cases is the syphilis and not the diabetes. Whether the new modes of treatment, especially with Ehrlich's dioxydiamido-arsenobenzol, will give us better results remains to be seen. Finally, in a large number of cases there can be no causal therapy, as no cause can be found during life and frequently no evidence of disease upon autopsy. It will be seen that at the present time the causal treatment of this disease offers us comparatively little. The reasons for this are many: We have been too much engrossed with the chemical aspect of the subject; physiology is just beginning to work out the relation of the various organs engaged in the production of dextrose. Moreover, cause and effect have been confused, because we know so little of the pathological physiology of this disease.

In by far the greatest number of cases, including dietetic treatment, as such, it is necessary to have recourse to symptomatic treatment, the results of which are measured by the amount of urine passed, its dextrose, acetones, and ammonia, by the time in which the urine may be made normal, and by the general condition of the patient. Dietetic treatment of diabetes mellitus produces increased carbohydrate tolerance; medicinal treatment, except in two instances, does not do this.

First among the medicines used is opium, introduced by Dobson in 1774 (von Mering), and now the only drug which is accepted by all writers on the subject of diabetes mellitus as doing good. Not any one of its alkaloids acts as beneficially as does the whole drug; whether Sahli's pantopon will do this remains to be seen. The effects produced by this drug in increasing doses are as follows: the quantity of urine becomes less; the sugar diminishes, notwithstanding the diet remains unchanged; thirst and hunger are lessened; and the patient may gain in weight. The objections to the use of this drug are: (1) That even while it is being taken its beneficial effects may disappear; (2) that sugar tolerance is not established by it; and (3) if discontinued, and then again prescribed it may or may not be followed by good results. It is administered as opium itself, of which 0.03 gram is given three times daily, increasing gradually to 0.5 gram for from one to three weeks. Naunyn states that in cases in which the quantity of urine is very great the dose may have to be increased to as much as 2 to 3 grams in a day. It seems that those cases are most benefited in which there is a nervous origin of the disease, so that, in so far as this may be the case, it may be looked upon as causal treatment. But I hasten to say that this is very rarely the case. The objections to opium are many; giving it to a patient for three weeks may be followed by the opium habit. I have seen this in two diabetic physicians. There are many human beings who cannot take opium in any form, and, after all, its

beneficial effects are limited. So that, as a rule, it should not be prescribed in every case, but only in exceptional instances, either in the rare nervous cases or when everything else has failed. In one of the physicians mentioned after the habit had been removed, the patient finally began to comprehend how necessary it was to follow dietary directions, and he continues as a mild diabetic, to follow his vocation eleven years after the outset of the disease. Von Mering⁵ uses the drug when he goes from a restricted to a severe dietetic régime, as it reduces hunger and the change is less felt. I have never found it necessary to do this, and would hesitate to follow this indication. Moreover, for reduction of nervous symptoms, it will be found that the bromides or antipyrin will take the place of opium in the great majority of cases.

For ordinary cases I prefer arsenic, and my experience has been the greatest with it. It should be given as liquor potassii arsenitis, in ascending doses, until mild toxic effects are produced; then the dosage should be gradually reduced. How it acts is difficult to say; it is known that paralysis of the bloodvessels of the splanchnic area prevents glycosuria; this follows toxic doses of arsenic; a congestion of this area also follows the use of smaller doses. However this may be, in order to get the best results from arsenic, mild toxic effects must be produced. It is probable that the neglect of this has caused disappointments in its effects, and at least the German authors ascribe no results as following its administration. The following case is one which illustrates its action:

A girl, aged twenty years; the father and mother are diabetics; she came under observation November 30, 1901. The following condition was present, and the following course ensued:

November 30, 1901. Sugar, 8 per cent.; quantity of urine, 3000 c.c.; acetone, a large quantity.

December 6. Sugar, 3 per cent.; quantity of urine, 2500 c.c.; acetone, plus.

She has not followed directions, which was the case before when under treatment. Although the sugar was reduced, she did not hesitate to admit that she was not going to diet strictly and that the reduction in sugar was due to a little care in diet. I then prescribed Fowler's solution and continued it, with the promise that she would be truthful as to indulgences in taking sweets. The quantity of urine was no longer measured, for obvious reasons.

December 10. Sugar, 2.5 per cent.; acetone, plus.

December 14. Sugar, 1.66 per cent.; acetone, minus.

December 30. Sugar, 1.66 per cent.; acetone, minus.

January 7, 1902. Sugar, 1.66 per cent.

January 15. Sugar, 1 per cent.; arsenic discontinued.

January 30. Sugar, 3.25 per cent.; acetone, plus; arsenic again given and pushed.

⁵ Von Penzoldt's Handbuch d. spec. Ther. d. inneren Krankh., ii, 90.

February 3. Sugar, 2.5 per cent.

February 17. Sugar, 3 per cent.

March 3. Sugar, 1.5 per cent.

March 13. Sugar, traces; arsenic discontinued.

March 17. Sugar, 1.33 per cent.

She was then taken to Germany, where she was put under the charge of several authorities upon diabetes mellitus. She was twice put into a sanitarium for antidiabetic treatment, and also took the cure in Carlsbad. From the written reports which were brought home she was never made sugar-free. Furthermore, the sugar percentages were never as low as they were when she was under the influence of arsenic, as noted before. On August 14, 1902, she again came under my observation, with 5.5 per cent., and large quantities of acetone.

August 18, 1902. Sugar, 6 per cent.; acetone, plus.

August 22. Sugar, 5.5 per cent.; acetone, plus.

August 26. Sugar, 6 per cent.; acetone, plus.

The cause of this complete failure of arsenic, which does not, as a rule, occur after it has been given for ten to twelve days, required investigation, and after much questioning it finally transpired that the young lady had engaged herself to be married. She had not had time to take her medicine, indeed, paid no attention to herself in any way. She consented to promise to do better. But she presented herself very rarely after this. When she did, the sugar was not less than 4 per cent. The last record is 8 per cent. sugar, acetone in enormous quantity. Diabetic coma developed, and death ensued December 10, 1902.

This patient, aged twenty years, with hereditary predisposition from both parents, passing large quantities of urine, which contained large quantities of sugar and acetone, and who never could be made absolutely sugar-free, presents the severest type of diabetes mellitus. The arsenic always caused reduction of the sugar.

This drug is especially indicated in the severe cases, but it should always be combined with diet. It may also be given for general indications, and it is very valuable in neurotic, debilitated subjects. Its beneficial effects here certainly contradict the statement of von Mering to the effect that "everything which impairs the appetite reduces the glycosuria." This drug does not increase sugar tolerance, and its effects gradually disappear when it is discontinued; unlike opium, never during its administration. Furthermore, in all of the patients I have treated, repeated courses have not lost their effect upon the glycosuria and diminution of acetone bodies.

The next two remedies to be mentioned are especially valuable in such patients in whom diet regulation is impossible. In another place⁶ I have stated how one of my medical friends, Dr. S. Stark,

⁶ The Prophylaxis and Treatment of Internal Diseases.

of Cincinnati, found that in a diabetic who had pyelitis, hexamethylenamine reduced the glycosuria. At the present time I have employed it for five years, and given it in 5-grain doses three or four times a day, which has been, in one instance, continually taken for four months without any bad effects. The following case will show its value:

A merchant, aged fifty years, has had diabetes for several years. He had had no results from treatment. The history was otherwise negative. He presented himself in June, 1908. The quantity of urine was 3000 c.c.; sugar, 2 per cent.; no acetone bodies. He was made sugar-free by von Noorden's diet. The sugar tolerance was calculated and an appropriate diet prescribed. June 2, 1908, quantity, 2000 c.c.; sugar, 1 per cent. He went to Carlsbad; came back in the autumn sugar-free and the tolerance much increased. Since leaving Carlsbad he has not dieted; in fact, he has made up his mind not to diet again. In March, 1909, he again presented himself: quantity, 2500 c.c.; sugar, 2 per cent.; no acetone; 0.30 gram of hexamethylenamine thrice daily was prescribed, and he remained practically free from sugar until October 1, 1909. Then again sugar (2 per cent.) was found, and increased quantity of urine. The sugar was reduced to 0.9 per cent. by belladonna. After two months, his sugar being kept down, he ceased to send his urine and passed from observation—he was tired of the restraint of doing anything for himself. On February 26, 1910, he again presented himself, having been to Carlsbad during the previous summer, and again suffering from his self-indulgence. The quantity was 3000 c.c.; the sugar, 4.5 per cent.; no diacetic acid. He cannot be made sugar free by diet, about 0.3 per cent. remaining. This again disappeared under hexamethylenamine by March 1, 1910. A third Carlsbad cure did not produce the usual effects. Dissatisfied with Carlsbad and with his doctor, he is treating himself.

With hexamethylenamine, glycosuria is improved and tolerance is increased. I would not recommend it for severe cases without proper diet. It is difficult to say how it does produce the results which are noted here. It has always been claimed that hexamethylenamine is excreted by the kidneys, being decomposed there into ammonia and formaldehyde. Lately some doubt has arisen in regard to this, but all agree that when this drug is administered, formaldehyde is found in the urine. From clinical experience we are justified in believing, at least until the contrary has been proved, that the same chemical change goes on in other places in the body. If this is the case, and formaldehyde is found in the blood, von Behring's statement, that formaldehyde is a complement saver, as he has shown for milk, might be considered as explaining its action in diabetes. The subject of the renal origin of diabetes can only be mentioned here; if it exists, and there is much evidence in its favor, the special value of hexamethylenamine, particularly when there is pyelitis, is of great importance.

Belladonna, which was condemned as useless by Frerichs in 1884, has again been recommended by Rudisch,⁷ and in such a convincing way that I have put a number of my patients upon this treatment. He recommends atropine methylbromide, beginning in adults with $\frac{2}{15}$ grain, three times daily, and increasing by adding $\frac{1}{15}$ grain until $\frac{8}{15}$ grain is given at one dose. He claims that this preparation is tolerated better than the ordinary preparations and is less toxic. Atropine sulphate, according to him, should be begun with $\frac{1}{150}$ grain, three times daily, and gradually increased to $\frac{1}{20}$ grain.

In as far as the medication itself is concerned, my results were the same whether I gave atropine methylbromide, atropine sulphate, or belladonna itself. It seemed to me that the tincture of belladonna was better tolerated than the other preparations. It is necessary, however, to get a reliable preparation, which has been difficult in my experience; and this, no doubt, is the reason why therapeutic failures occur so frequently when this drug is prescribed in this form. The results which I have obtained, aside from what has been stated, agree fully with those of Rudisch. In a large number of cases glycosuria, and with it acetone bodies, have diminished or disappeared and carbohydrate tolerance was increased. Indeed, some of the patients were not dieting when taking this remedy, but when it was discontinued the sugar did not reappear for some time. In several severe cases it did no good. It seems perfectly adapted to milder cases, so that in one instance, without diet, there has been absence of sugar for over a year. In one case of diabetes in a child the disease ran its usual course, notwithstanding a strict adherence to Rudisch's directions as to diet and atropine methylbromide.

The views regarding the effects of mineral waters on this disease, and I refer especially to Carlsbad and Vichy, differ much. Most excellent observers state that the effects are negative (von Mehling); others hold the view (von Naunyn) that they are beneficial only in mild cases; and the fewest number of authors state that they are of value in every case. The latter view can be dismissed without discussion. The former view must be considered. It is based largely upon the theoretical assumption and experimental experience that alkalies have no effect upon dextrose elimination when given in the form in which they appear in the mineral waters before mentioned. It does not matter whether Glauber's salt with or without other alkalies, Carlsbad salts (artificial or "natural"), or bottled Carlsbad water has been used in coming to this conclusion; the results of such experiments are absolutely inconclusive in regard to the effects of these waters when taken as they flow from the spring. Physical chemistry has shown that all the other analyses which we have considered as final are imperfect in so far as they prevent a conception of the inner ionic structure of mineral waters, so that all the experiments

⁷ Medical Record, June 26, 1909.

made before this was discovered are inconclusive and without value. Among those who claim that Carlsbad is beneficial, there are those who attribute the good effects to change of scene, rest, change of surroundings, and diet. The benefits of the first three in diabetes will be admitted by all. So far as the diet is concerned, until within the last few years there was not enough stress laid upon it in Carlsbad. In 1906 Naunyn wrote: "It is certain that the success of the cure at these various places does not depend upon a specially strict dietetic treatment; according to my experience, one cannot count with certainty upon a strict dietetic treatment." That this is true there is no doubt, but, fortunately, things have changed somewhat in Carlsbad, so that the patients can be, and are, dieted there as strictly as anywhere. Experience teaches us that good results are obtained there which are not due to diet and external conditions; therefore, it would seem that the waters do play a role in the production of these results. What has been said of Carlsbad is also true of Neuenahr and Vichy. In a few places in our country rational dieting is also being introduced.

In the new conditions which obtain in Carlsbad both mild and severe forms are improved by treatment. Naturally, the mild forms are improved most, and while the older statements in regard to the inefficiency of these cures may have been true, at present even severe forms may improve there. Being of the severe form, these patients do not come home sugar free, but with sugar reduced and their general health much improved. In the milder cases sugar disappears, tolerance is enormously increased, and the general condition is improved. In a number of cases the sugar tolerance persists for as long as six months, notwithstanding the fact that these patients do not diet. The mildest cases, when their diet is arranged for their sugar tolerance, may remain sugar free for years. It is true that this does occur without Carlsbad with the ordinary diabetic treatment, but it is my experience that it does not occur so frequently. The case reported before with hexamethylenamine treatment illustrates this very well.

For treatment, only one complication, diabetic coma, need be considered here, as all the others either disappear when the glycosuria is controlled or are treated as they would be in other circumstances. At present, diabetic coma is looked upon as an acidosis, due to the presence of large quantities of oxybutyric and, possibly, diacetic acid in the blood—the result of which is that first the ordinary alkalies are bound to them for elimination by the urine, and when these are no longer sufficient, ammonia is formed from ultimate metabolic changes of albumin which ordinarily leads only to urea. This ammonia combines with the harmful acids and is found in the urine. Indeed, the amount of ammonia found in the urine may be looked upon as a quantitative estimate of the acidosis. From this it would seem that the solution of this therapeutic problem

should be easy; add alkalies to control the acids. As a matter of fact, this is what has been done. Sodium carbonate or bicarbonate have been administered by the mouth, the rectum, and intravenously in large quantities, varying from 15 to 84 grams in twenty-four hours. And yet, simple as is the ratiocination, this treatment has remained singularly ineffective. I have never seen a patient recover from true diabetic coma when it has been thoroughly established. I have seen diabetics recover from coma due to other causes, as has everyone who has seen many diabetics, and this line of demarcation between coma in diabetes and diabetic coma should be carefully drawn in the reports of cases. Moreover, even when one neutralizes the urine, the coma being developed, the patient does not recover, which shows that eventually this whole process is something more than a simple question of acidity and alkalinity. The urine, being more alkaline, shows that in all probability the blood is also alkaline. But we have no evidence that the tissues are favorably affected by this alkalinity or that the alkalinity is of the proper nature. To overcome this, it might be well to try other ions beside those of sodium when diabetic coma is well developed. But even this seems hopeless when we consider that tissue changes go on which probably are irremediable, because of the time required to remove them.

On the other hand, when the first symptoms of coma are recognized, the therapeutic results are fairly good with sodium treatment. The indications for the administration of sodium bicarbonate are the occurrence of large quantities of acetone or ammonia in the urine. This should always be followed by the internal administration of sodium bicarbonate in quantities sufficient to make the urine neutral or slightly alkaline; when the remedy is withdrawn and the previous urinary condition again develops, the indication should again be carried out. In addition, the patient should be put upon the proper diet. For practical purposes, it may be accepted that fats and albumin principally produce acetone bodies and acidosis; therefore these patients should be put upon carbohydrates, irrespective of the degree of glycosuria, as the prevention of the full development of diabetic coma is, for the time being, the paramount indication. Large quantities of oatmeal or potato may be given, but according to Naunyn's experience, which I can verify from personal experience, milk in sufficient quantity as an exclusive food seems to be the best that can be done dietetically. I cannot refrain from again stating the fact that in treating diabetics for sugar tolerance great care must be taken not to produce coma. This does occur, and it is not a pleasant experience. There are two ways to avoid it: the first is by taking into consideration the results of urine analysis, as stated before, the second is to give patients sodium bicarbonate during the testing period, as was first recommended by von Noorden.

THE DIETETIC TREATMENT OF DIABETES MELLITUS.

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To one who has devoted much attention to the study and treatment of diabetes the difficulties that beset the general practitioner in an endeavor to arrange diets for these cases and to make the requisite analyses within the time available seems almost insurmountable. It is the object of this paper to present in a simple way such routine procedures as a clear understanding of the individual case demands and a scheme of diet tables which permits of that adaptation of food to the peculiarities of the individual without which no degree of success can be expected. The dietetic treatment of diabetes demands the same attention to detail that is required in the modification of milk for infant feeding, and on this account minutiae will be set forth in this paper which to many will appear unnecessary.

Before proceeding further it is desirable to say a word regarding the detection of sugar in urine. When large amounts of sugar are present in the urine there is no likelihood of other substances being mistaken for it; but when less than 1 per cent. occurs this is not the case if Fehling's solution be employed, as it now generally is. I have seen three persons who had been told that they suffered from diabetes and who excreted no sugar in the urine, the reducing body being glycuronic acid. It should be remembered that reducing bodies other than glucose react with alkaline copper solutions; of these uric acid, glycuronic acid, and sugars other than glucose may occur in the urine in amounts large enough to lead to confusion. A urine which reduces Fehling's solution before, but not after fermentation, in all probability contains glucose. Occasionally one finds that the urine passed at one time of day has a little glucose in it, while none may be found in other samples from the twenty-four hour specimen. This is rather characteristic of a type of gouty individual; and the sugar excretion in such cases will be found to follow a meal when it is the man's habit to eat largely of sweets. For example, one patient had sugar in the urine passed during the night and it was found on inquiry that he usually ate considerable candy after dinner. These cases are not to be regarded as diabetics, although some of them doubtless become so. They should be cautioned and the total amount of food diminished, since they are always over weight.

In advising a diet for a diabetic, one has the following conditions to consider: (1) A diminished ability on the part of the diseased organism to assimilate carbohydrates; (2) a metabolism perverted in such a manner that fatty acids are no longer burned in a normal

manner or to their normal end-products and in consequence of this acid bodies are developed which are toxic; and (3) a diminution of carbohydrate food to meet condition (1) predisposes and increases in degree condition (2). From these considerations it is evident that whatever is done in the way of diminishing the carbohydrate ingest must be effected with caution and with attention directed as much to the degree of acidosis as to the sugar output. On this account it is always advisable to change from a general diet containing a normal amount of carbohydrate to one that is poor in starch gradually; and this is especially the case with young patients. This aim is most easily effected by having some routine diet containing a definite and known amount of carbohydrate which may be gradually reduced as one proceeds with the case in hand. It is an advantage to begin with such a diet in each case because the differences of "reaction" give clues as to what may be expected from various therapeutic and dietetic procedures. The following is the diet I employ as a means of finding the type to which an individual case belongs:

"TEST" DIET.¹

Breakfast:

- 3 eggs with 25 grams of bacon.
- 3 biscuits (Huntly and Palmer breakfast²) with 20 grams of butter.
- 1 cup of strong coffee,³ 25 c.c. of cream.

Dinner:

- 1 cup of bouillon.
- 100 grams of beefsteak or roast beef (weighed cooked).
- Boiled cabbage or cauliflower with butter sauce ad libitum; lettuce with oil and vinegar.
- 25 grams of cream cheese.
- Coffee jelly with 25 c.c. of cream.
- 3 biscuits with 20 grams of butter.

4 to 5 P.M.:

- Coffee or tea with 25 c.c. of cream.
- 1 biscuit; 10 grams of butter.

Supper:

- 100 grams of fish (weighed cooked).
- 2 eggs.
- Asparagus as salad or hot (with butter sauce).
- 3 biscuits; 20 grams of butter.
- 1 dozen almonds.

This diet represents approximately 125 grams of protein and 100 grams of carbohydrate, and is equivalent to 3200 calories. It would be more than adequate were it not for the sugar loss through the urine, which for the time must be made good to prevent loss of weight.

¹ Without bread this diet is practically free of sugar and is the "C. F." (carbohydrate-free) diet of these tables; variety is secured by changes from Tables A and B.

² Any bread or cracker that can be secured of uniform size and composition will serve as well.

³ Crystalline is superior to saccharin as a substitute for sugar.

The patient should be restricted absolutely to this diet, for two days, the urine being collected during the *second* twenty-four hours, and estimations made for the quantity of glucose and the presence and approximate amounts of diacetic and β -oxybutyric acids.⁴ The next step in the diet arrangement will depend exclusively upon this analysis, and it will serve best for clearness if concrete cases be used for illustration. The analysis may show any one of the following conditions:

1. Sugar less than 100 grams, ketone bodies in small amounts.
2. Sugar more than 100 grams, ketone bodies in small amounts.
3. Sugar less than 100 grams, ketone bodies in large amounts.
4. Sugar more than 100 grams, ketone bodies in large amounts.

A case representing the features of the first postulate still retains considerable ability to assimilate carbohydrate (less being excreted than the amount in the food), and is not suffering from acidosis. This is perhaps the least difficult type to deal with, and one in which success is probable. These patients are usually past middle age and the occasion for consulting a physician is the inconvenience of polyuria, pruritus, carbuncle, etc. The method to be observed in treatment is illustrated by the following case:

CASE I.—Mrs. E. C. G., aged fifty-six years.

			Urine.	Sugar.		Diacetic	β -oxy-	
			Amount.	Amount.	Acetone.	acid.	butyric	Weight.
		Diet.	c.c.	Grams.	Grams.	Grams.	Grams.	Pounds.
1907								
March	3	"Test"	1850	47.5	1.5	Trace	0	181
"	4	"C. F."	1920	38.0	1.8	Trace	0	
"	5	"C. F."	1570	11.0	Trace	0	0	
"	6	"C. F."	1580	Trace	Trace	0	0	180
"	7	"C. F."	1250	None	Trace	0	0	
"	8	"C. F."	1340	None	Trace	0	0	
"	9	"C. F."	1270	None	None	0	0	
"	10	"C. F."	1360	None	None	0	0	181
"	11	50 grams bread	1370	None	None	0	0	
"	12	50 grams bread	1290	None	None	0	0	
"	13	50 grams plus	1310	None	None	0	0	182
		25 grams						
equivalent in Table C.								

equivalent in Table C.

For the following ten days a choice was given of either 75 grams of bread or its carbohydrate equivalent in Tables C and D; at the same time substitutions were made in the "Test" diet for the meats

⁴ The polariscope should not be depended upon for estimating sugar in diabetic urines as the error introduced by the presence of diacetic acid may be very considerable. There are modifications of the titration methods that make it possible to secure more accurate results than the polariscope gives and that require no more time or skill. Benedict's modification of Fehling's solution works admirably with a very sharp end point. The method will shortly be published in the *Journal of Biological Chemistry*. Citron's method or Gerhart's are quickly and easily done. The determination of ketone bodies is an operation that demands considerable laboratory apparatus and some experience in chemical processes; no method thus far devised yields better than approximate results. Quite as much information—if not more—can be gained from ammonia estimations which are easily made and require very little apparatus or skill.

and vegetables (Tables A and B) to give variety to the food. During this period no sugar appeared in the urine. The patient was then directed to send a twenty-four hour specimen of urine every third day and to continue the use of the diet which was by this time clearly understood by her. It will be noted that with abstractions from these tables suited to the locality and season the patient is given considerable latitude, and yet the carbohydrate fraction is kept within pretty definite limits.⁵ It was found possible within the next two months by slowly increasing the allowance of carbohydrate, first to 85 grams, then by 10 gram increments, to allow 120 grams daily without sugar appearing in the urine. No attempt was made to arrive at a higher tolerance. This patient was in good health a year later and no sugar was excreted in the urine:

As an illustration of the second type in the classification (sugar more than 100 grams; ketone bodies in small amounts) the following case will serve us:

CASE II.—F. B., aged forty-two years. He has had diabetes three years, and has lost much in weight; of late he has been unable to work on account of weakness.

Date.	Diet.	Urine. Amount. c.c.	Sugar. Amount. Grams.	Diacetic acid. Grams.	β -oxy- butyric acid. Grams.	Weight. Pounds.
Feb. 8	"Test"	3100	186.0	None	None	104
" 9	75 grams bread	2800	111.0	None	None	
" 10	75 grams bread	2500	93.0	None	None	
" 11	"C. F."	1160	25.3	None	None	
" 12	"C. F."	1170	20.9	Trace	None	106½
" 13	"C. F."	1250	12.1	4.4	Trace	
" 14	Oatmeal	1180	29.4	2.3		
" 15	Oatmeal	1210	20.0	None	None	
" 16	Oatmeal	1240	1.3	None	None	
" 17	Oatmeal	1190	None	None	None	106½
" 18	Breakfast, oatmeal and cream	1070	None	None	None	
" 19	Lunch and dinner.	1290	None	None	None	
" 20	"C. F." + 50 grams oat cakes. ⁶	1185	None	None	None	
" 21		1240	None	None	None	109
" 22		1220	0.9	None	None	
" 23		1140	None	None	None	
" 24		1030	None	None	None	109
" 25		1280	None	None	None	
" 26		1265	None	None	None	

It will be noted that at the beginning of the treatment there seemed to be no tolerance for carbohydrates, much more being eliminated in the urine than could be accounted for in the diet. On a carbohydrate-free diet, however, the sugar excretion rapidly fell and it appeared that the urine would have been free of glucose in a few days had the diet been continued. With the diminution in sugar

⁵ A suitable balance with weights may be purchased for about \$5.00.

⁶ Receipt for preparation at end of this paper.

excretion, however, there was an increase in acetone and diacetic acid, and the patient's condition suggested that more acids were retained than were excreted. At this juncture (February 13) two lines of procedure were open: (a) Alkalies might have been used to aid in the acid elimination and the same diet continued. Under these conditions—a falling sugar excretion with a slight grade of acidosis—the ketone bodies often disappear from the urine along with the sugar; the explanation apparently being that with regained ability to burn sugar the normal metabolism of the acids takes place also. In many cases small doses of alcohol at this time help to the desired end. The other alternative in treatment was, (b) the use of oatmeal, which is one of the surest means of combating acidosis and in many cases also decreases the sugar excretion as well. (The details of the oatmeal "cure" will be entered into later in this paper.)

This diet—oatmeal and cream for breakfast; lunch and dinner from Tables A and B, plus 50 grams of oat cakes—was continued for two weeks, February 18 to March 4; then 40 grams of white bread was allowed on alternate days, but one day in each week was kept carbohydrate-free, neither bread nor oatmeal being permitted. As no sugar appeared in the urine during this experiment and the patient liked the diet he was ordered to continue its use indefinitely; the carbohydrate-free diet list given him being made up of Tables A and B. His urine showed sugar but twice during the next three months, analyses being made every third day. He then left town and was lost sight of.

The object of reserving one day at fixed periods on which no carbohydrate is to be eaten, is that by so doing the tolerance for carbohydrate is not strained. It is, so to speak, a rest day for a special function. The indication for this occasional rest is shown in the fact that amounts of starch which are metabolized perfectly at the commencement of a given diet, may after an interval, induce a glycosuria, at first slight but daily increasing until the larger part of the carbohydrate eaten is promptly excreted.

It occasionally happens, of course, that oatmeal is not well tolerated in cases of the above type, the sugar output increasing rather than diminishing after its use. This, in my experience is exceptional; an initial rise in the sugar excretion is common, but in a few days it rapidly subsides. When, however, oatmeal is found detrimental, the method already mentioned is usually effectual in patients past middle life—carbohydrate-free diet, with alkalies to combat mild acidosis. After there is no longer loss of glucose through the urine we must proceed to build up a dietary by adding small known amounts of starchy foods, as in the cases already described, keeping these amounts within the assimilation limit of the patient and interpolating at definite periods carbohydrate-free days to aid in preserving any tolerance established.

With patients younger than the last case the difficulty is usually not so quickly nor easily overcome, although the acidosis may not be alarming early in the course of the disease. The next case to be considered comes under the same classification as the last one—sugar excretion more than 100 grams, ketone bodies in small amounts—but is much more severe and intractable to treatment.

CASE III.—S. A., aged twenty-nine years; complains of thirst and weakness. In May, 1908, he noted that he was losing flesh and strength. He improved a little during the summer without seeing his physician. He was refused insurance in September, 1908, and was told he had diabetes. He has lost about forty pounds in eight months. He has a splendid appetite, and drinks over a gallon of water a day.

Date.	Diet.	Urine. Amount. c.c.	Sugar. Amount. Grams.	Diacetic acid.	β -oxy- butyric acid.	Weight. Pounds.
Jan. 1	Standard	4200	310	++	None	112
" 2	"C. F." + 75 grams bread	3400	287	++	None	
" 3	"C. F." + 75 grams bread	1500	111	+	None	
" 4	"C. F." + 35 grams bread	1900	129	+	None	
" 5	"C. F." + 35 grams bread	2000	112	+	None	112½
" 6	"C. F." + 35 grams bread	3400	122	Trace	None	
" 7	"C. F." + 35 grams bread	1400	74.3	Trace	None	
" 8	"C. F." + 35 grams bread	1380	81.0	Trace	None	
" 9	"C. F." + 35 grams bread	1850	70.4	Trace	None	114
" 11	"C. F." (No bread)	2400	79.0	Trace	None	
" 13	"C. F." (No bread)	2475	81.6	+	None	
" 15 }	17th & 18th "green	2100	63.0	Trace	None	
" 18 }	days"	1450	15.5	+	None	115½
" 21 }	19th, 20th & 21st					
" 24 }	oatmeal days	1450	29.0	+	None	
" 24	"C. F." + oat cakes, 30 grams	500	2.5	+	None	
" 26	"C. F." + oat cakes, 30 grams	600	None	Trace	None	
" 27	"C. F." + oat cakes, 30 grams	950	8.5	+	None	
" 28	"C. F." + oat cakes, 30 grams	2470	9.9	+	None	115½
" 29	+ 20 grams bread	2100	8.4	+	None	
" 30	+ 20 grams bread	3100	27.8	Trace	None	
" 31	+ 20 grams bread	2300	18.4	+	None	
Feb. 1	+ 20 grams bread	1775	19.5	+	None	
" 6	20 grams bread	1800	20.6	+	None	
" 9	20 grams bread	1950	8.0	+	None	
" 15	20 grams bread	2100	17.0	Trace	None	
" 21	20 grams bread	1710	None	None	None	
" 27	20 grams bread	1690	3.4	None	None	126
March 3	40 grams bread	1480	None	None	None	
" 15	40 grams bread	1520	None	None	None	135

It is to be noted here that sugar was still excreted in large amounts after five days of starch-free diet (January 10 to 15) and that three "green days" did not rid the urine of sugar. There was a rapid fall when small amounts of oat cakes were allowed along with the carbohydrate-free diet, but an immediate rise when wheat bread was substituted; indicating that only a very slight tolerance existed. The sole encouraging feature in the case was that the acidosis remained an almost negligible factor. Inasmuch as with young individuals exemplified by this case there is a marked tendency to acidosis, which must be constantly had in mind, it was not advisable to withhold starch from the diet for any prolonged period. On that account the following routine was advised to be continued for one month: One day, foods from Tables A and B, plus 30 grams of bread; two "green days;" and one oatmeal day. These days were to alternate in their above order, bread day, "green days," oatmeal day, then bread day, and so on. The urine was collected during each "bread day" which represented the maximum excretion of sugar it was found. The object of this arrangement of diet was to reduce sugar excretion by means of the "green" day and "oatmeal" day; to counteract any tendency to acidosis arising from the starvation of the "green days" by the oatmeal day and to keep up the general nutrition if possible, by means of the more liberal "bread" day. The result was so satisfactory to the patient at the end of the month that he desired to continue in the routine a while longer. At the end of three months the amount of bread had been gradually increased to 90 grams without sugar in the urine. This with its equivalents (Table C) made a considerable relaxation from the strictness of the diet on the other days.

In a case like the above nothing can be accomplished, nor should be expected, without the full coöperation of the patient. The diet, at best, is irksome and a fixed routine most disagreeable to many temperaments. Still there are but a few of the laity who do not realize something of the gravity of the disease, and this together with the amelioration of the torment of constant hunger and thirst and the increase in strength and sense of well-being render the majority of patients eager coöperators with their physician.

One word here with regard to what may be hoped for in diabetics like the last case. A minority develop after a year of treatment considerable assimilative power for carbohydrates—100 grams of bread. This is often retained for several years, but eventually becomes broken down either because of their own disregard of directions or of a too optimistic medical adviser. The majority even under strict supervision slowly lose their tolerance and in the course of a few years arrive at a condition where little if anything can be done for them. The benefit of treatment is solely in postponing the latter state and prolonging for a period some semblance of health compatible with activity and enjoyment. Very exceptionatly, I think, these cases live for a decade or over even though the disease

has begun when the patient was under thirty. I have knowledge of but one such case, a man who first learned of his diabetes when he was twenty-four and died at the age of forty.

The class of diabetes in which acidosis is a prominent symptom demanding constant attention and regulation of diet next requires attention. These cases for the most part are to be regarded as a later stage in the type already discussed and the greatest care is demanded by the younger patients, since they not only develop alarming grades of toxemia very quickly but also withstand it poorly.

The following case is an example of this type:

CASE IV.—J. B., aged twelve years. The patient was a healthy girl until about a year ago when she began to have great thirst, an abnormally increased appetite, and to lose in weight. The family physician found sugar in the urine and ordered a diabetic diet, which caused the child to improve for a while, but she soon was as bad off as before, and the parents in consequence brought her to the hospital. On admission the child looked flushed and toxic, and the first urine voided was found to give an intense reaction for diacetic and β -oxybutyric acids. Oatmeal diet was directed in an amount sufficient to give adequate calories for nourishment: oatmeal, 6 ounces; butter, $1\frac{1}{2}$ ounces; 2 eggs; water, 24 ounces; 6 ounces of this gruel was given every four hours.

Date.	Diet.	Urine.	Sugar.	Acetone	β -oxy-	Nitro-	Ammono-	Weight.
		Volume.		+ diacetic	butyric acid.			
		c.c.	Grams.	Grams.	Grams	gen.	nia.	Pounds.
March 10	Oatmeal	2700	175.0	1.47	2.65	12.89	2.02	51
" 11	Oatmeal	1400	70.0	1.18	1.70	8.51	1.40	
" 12	Oatmeal	780	15.6	0.18	0.11	3.9	0.80	
" 13	Oatmeal	850	0.8	0.40	0.38	7.6	0.81	
" 14	Oatmeal	760	Trace	0.25	0.21	7.1	0.80	52
" 15	"C. F."	810	None	0.19	0.26	9.1	0.86	
" 16	"C. F."	840	Trace	0.17	0.25	9.7	0.88	
" 17	"Green day"	790	None	0.28	0.20	6.9	0.92	52½
" 18	Oatmeal	750	Trace	0.20	0.13	7.5	0.81	

It is unnecessary to continue the table further, as the above gives an adequate idea of the patient's condition. The urine could not be freed of sugar for more than a day at a time, because the necessary restrictions induced a prompt increase in ketone bodies. All that was accomplished in the above case after a month's treatment was a gain in weight and a marked increase in sense of well-being to the patient. No substantial tolerance for carbohydrate was established nor could be expected. If we can make such individuals comfortable we must be satisfied in the present state of our knowledge and by doing so we are able to prolong life. The following case was one of the most severe I have seen, and from the first hopeless, yet the child was kept sufficiently well to enjoy life until the day before she died—a period of two and a half years.

CASE V.—C. G., aged four years, was brought by her father who also had diabetes and had had Graves' disease. Sugar was first found in the child's urine in December, 1907. At first, by careful supervision, the urine was kept almost constantly sugar free during the winter and spring of 1907 and 1908, allowing 25 to 30 grams of bread. At this time there was no tendency to acidosis. During the summer of 1908, no sugar was excreted for sixty days, but the tolerance had diminished, as it continued to do gradually until in October, 1908, a carbohydrate-free diet was necessary to secure glucose-free urine. On a diet of 8 grams of rice in the morning and 8 grams of zweiback at noon and night, 7 grams of glucose appeared in the urine. A slight grade of acidosis first made its appearance at this time, but a satisfactory condition was maintained until January, 1909. Then, coincident with otitis media an alarming degree of acidosis suddenly developed, as evidenced by symptoms and urine analyses. Ten days of exclusive oatmeal diet was necessary to carry the patient through this complication. Following the recovery from the otitis media it was found that the glucosuria could be controlled only by the use of "green days" in alternation with oatmeal days for the acidosis. The routine was one vegetable day followed by two days of liberal diet on which definite amounts of starchy foods were allowed. Then again a vegetable day, two oatmeal days, a vegetable day, and so on. With this regimen the patient regained the weight lost during the acute illness and appeared very well until early spring of 1909. From April, 1909, the urine could not be longer freed of sugar and the amount of ketone bodies excreted seemed to threaten toxemia, although the child appeared quite well usually and played with other children a large part of each day. Oatmeal no longer produced any effect on the glycosuria and because of abdominal distention and pain, which it appeared to induce, was abandoned as a gruel and used only as cakes with other food.

Date.	Diet.	Urine. Amount. c.c.	Sugar. Amount. Grams.	Acetone + diacetic Grams.	β -oxy- butyric acid. Grams.	Total N.	NH ₂ N.
Oct. 19, 1908	8 grams rice and zweiback 16 grams	800	6.21	0.55	0.14	7.1	0.70
Apr. 22, 1909	Vegetable day	1260	13.40	0.29	0.38		
" 26,	Oatmeal	3240	106.4	1.88	0.20		
" 29,	"C. F." + levulose apples	2935	85.1	3.25	5.88	11.44	2.39
May 2,	Oat cakes	2400	84.9				
" 6,	Oat cakes + apples	2520	64.7	2.69	4.16	9.12	2.22
" 12,	Graham cakes + apples	1830	67.7				
" 20,	Oat cakes	2500	46.0	4.35	4.74	10.44	2.12
" 26,	Oat cakes	2490	65.0				
June 7,	Oat cakes	3200	81.0				
" 20,	Oat cakes	2500	48.2	2.93	6.96	11.15	1.88
July 5,	Oat cakes, alkalies	2000	50.0	3.06	3.70	6.01	1.42
" 10,	Oat cakes, alkalies	2300	98.9			3.84	0.55
" 14,	Oat cakes	2000	106.0	3.14	6.52	3.24	0.58

Coma supervened on July 20 and resulted fatally on the following day. Infusion with alkalies was not considered on account of the hopeless condition of the child before coma began. This case represents the severest and most desperate manifestation of diabetes, especially when it occurs in so young a person. And it must be confessed that this child owed her two years of life as much to the intelligent care and resourcefulness of the mother as to her physician.

The cases that have been cited serve to show the methods that may be employed to meet definite indications. I have called them typical, but it is to be understood that type is meant only in the gross sense. Every case of diabetes is peculiar in some or perhaps all of its features and so there are no types in an exact sense. The secret of treatment is the individual treatment, the adaptation of methods to the peculiarities of each case. There is no diet adapted to all, not even to all of a gross type.

ACIDOSIS. As acidosis is the complication most to be feared in every case of diabetes the subject demands more than a passing word.

Despite every care that we know how to exercise, many diabetics develop a severe degree of acidosis which sooner or later terminates life. It is not yet clear whether the development of ketone bodies is to be interpreted as an entirely abnormal type of metabolism, or whether these substances are intermediate metabolic products which the diseased organism cannot split in the normal manner to their proper end products: CO_2 and water. The source of β -oxybutyric acid (the mother substance from which diacetic acid and acetone are derived) is mostly from the fatty acids. It is conceivable that any straight chain fatty acid with an even number of carbon atoms in its molecule may break down into butyric acid, and for many such acids the fact has been demonstrated. In a less degree, but doubtless to some extent, protein may also give origin to the ketone bodies, since the amino-fatty acids are readily disamidized in the body and are then to be regarded as simple fatty acids.

As a usual thing, it is far easier to postpone the initial development of acidosis than it is to cope with the pronounced condition once it has become fixed. But I am convinced that the feeding of carbohydrate food when such food is not assimilated, but passes through the body into the urine does not in any way delay acid toxemia. Carbohydrates that are burned, on the contrary, do prevent acidosis, causing the acids, it may be, to be burned also. It is for this reason probably, that the oatmeal diet acts so well in many cases of acidosis. The carbohydrate in this case is burned, and in those individuals who retain for some time a carbohydrate tolerance, it is to be noted that the acidosis does not reach an alarming degree until such tolerance has utterly failed. There are

some features of this intoxication that find analogies in inanition; for example, the excretion of ketone bodies reaches a surprising extent in many cases of gastric ulcer under the von Leube treatment.

When no bread or its equivalent can be allowed without the appearance of corresponding amounts of sugar in the urine the interpolation of oatmeal days is the best way to proceed. Later in the course of the disease several such days may be necessary and in a few cases I have ordered this diet unremittingly for two weeks. In some cases the appearance of ketone bodies in the urine may be quickly checked by the addition of alcohol in some form to the dietary.⁷ In these, strange as it may seem, the tolerance for carbohydrate appears improved by this measure.

This is perhaps as good a place as another to speak of levulose. As is well known, some diabetics can assimilate this sugar when not able to use any other, and on this account it has been much over-used by physicians. The tolerance for levulose is never large and is invariably short lived if the sugar be constantly eaten. On that account it should be employed in small amounts and never constantly. In Germany, a levulose chocolate is much used as a confection for diabetics and satisfies that hunger for sweets which many have. It is also convenient with fruits, apples, cranberries, currents, to manufacture marmalades and preserves. Levulose, if used discreetly, is a valuable aid in preventing acidosis, but it is an aid only so long as it is metabolized.

In spite of the best of care the majority of the younger cases of diabetes will sooner or later develop severe grades of acidosis, evidenced not only by the ketoneuria but by loss of appetite and somnolence. For this, besides the diets already mentioned, we have to resort to large doses of alkalies, sodium bicarbonate alone or mixed with a quarter to half its weight of citrate. Some patients prefer to take the alkalies in capsules, others find them not too unpleasant when dissolved in water.

A final word with reference to infusion with alkalies in diabetic coma. Enormous quantities of alkalies are often required to produce any effect. It is advisable to use 4 per cent. sodium bicarbonate solution and to repeat the procedure until 100 grams has been administered. As soon as possible, if consciousness returns, alkalies should be given by the mouth also. The length of life following a successful treatment of coma is in the vast majority of cases so brief that the operation is not suited to every case. It hardly seems justifiable, for instance, in the case of children when all that may reasonably be expected is a few days more of precarious existence.

DIET TABLES. In an attempt to arrange a dietary for a diabetic it is necessary to give as much variety in foods as possible. If this be not considered the patient becomes disheartened with the restraint,

⁷ This was first called to my attention by a case of Friedrich von Müller at his Munich clinic

the appetite fails, and he loses in weight and strength. In the following tables the effort is made to gain the greatest possible variety and at the same time to control absolutely the carbohydrate ingest. Tables A and B are made up of foods that are nearly carbohydrate free and from these lists this sort of dietary may be constructed according to the patient's preferences. These foods (Tables A and B), may be used without restriction of quantity unless there is a necessity of limiting the amount of protein consumed. In Tables C and D the foods all contain carbohydrate. These tables are to be used only when the carbohydrate tolerance of the patient is known, and then the total amount of starch-containing food should be kept well below the tolerance limit (by at least 10 grams of bread). For example, if 60 grams of white bread is assimilated without inducing glycosuria, then not more than 50 grams in equivalents should be allowed. Further, foods like potatoes and fruits should be separately tested with each patient in order to determine whether there is any peculiarity of reaction toward them respecting sugar excretion.

The order and number of meals requires consideration also; four or five meals are better than three; a second breakfast and afternoon tea may be interpolated. Half of the daily allowance of bread should be taken at the mid-day meal and it is better that at least a third of the daily bread allowance be used as equivalents—vegetables and fruits.

TABLE A.

Fresh Meats: All muscle parts of beef, veal, pork, lamb, mutton, domestic, and wild fowl, either roasted, boiled, or broiled, in their juices, with butter, or with mayonnaise made without flour, either hot or cold.

Various Organs of Animals: Tongue, heart, brains, sweetbreads, kidneys, marrow, calves' liver, liver of game or poultry (pate de fois gras) up to 100 grams in weight, weighed after being prepared.

Preserved Meat: Smoked meat, dried meat, smoked or pickled tongue, ham or bacon, corned beef, sausage (containing no bread). Be sure that no flour is used in preparing pickled meats.

Meat peptones of all kinds, jellies, or aspics prepared from calves' feet, or pure gelatine; nutrose, tropon, plasmon, wheat gluten, etc.

Fresh Fish: All fresh fish boiled, fried, or broiled. If the fish is fried in bread crumbs and eggs the crust should be removed before the fish is eaten. All sauces that contain no flour are allowed; those that contain butter and lemon are the best.

Preserved Fish: Dried, salted, and smoked, such as haddock, cod, herring, mackerel, flounder, sturgeon, eels, salmon, etc. Pickled herrings, sardines in oil, mackerel in oil, anchovy, tunnyfish, etc.

Fish Products: Caviar, cod-liver oil.

Shell Fish and Crustacea: Oysters, clams, and other shellfish, lobsters, crabs, crawfish, shrimps, turtle, etc.

TABLE B.⁸

Foods Rich in Fats: Dairy products—cream, butter, yolks of eggs, cheese.

Animal fats—bone marrow, fat of edible meats, lard, tallow (used in cooking), cod-liver oil, oleomargarine. *Vegetable fats*—olive oil, cottonseed oil, peanut oil, peanut butter, nut butter.

⁸ These tables are based on the composition of foods as given in Bulletin 28, United States Department of Agriculture, and on the Nahrungsmittel Table of Schall and Heisler.

Vegetables containing a slight amount of carbohydrate (less than 4 per cent.). These may be taken in normal quantities unless otherwise directed: Asparagus, 2 per cent.; beet greens, 3.2 per cent.; Brussels sprouts, 3.4 per cent.; cabbage, 4.8 per cent.; celery, 3.3 per cent.; chard, 3.4 per cent.; cucumbers, 3.1 per cent.; endive, 2.2 per cent.; lettuce, 2.9 per cent.; sauerkraut, 3.8 per cent.; spinach, 2.8 per cent.; string beans, 1.9 per cent.; tomatoes (fresh), 3.9 per cent.

TABLE C.—Foods Containing Carbohydrate and to be Used Only in Restricted Quantity.

	Grams.	Grams.	Grams.	Grams.
	10	20	30	50
White bread	Equivalent to	Equivalent to	Equivalent to	Equivalent to
Corn bread	12	24	35	60
Graham bread	10	20	30	50
Gluten bread	13	26	39	65
Oat cakes	25	50	75	125
Wheat flour	8	16	24	40
Hominy (boiled)	20	38	50	
Rice (boiled)	14	28	42	
Tapioca (pudding)	15	30	45	
Macaroni (cooked)	30	60	90	
Spaghetti (cooked)	30	60	90	
Cocoa (unsweetened)	12			

Vegetables:

Asparagus (cooked)	175	350 ⁹		
Beans, red kidney	25	50		
Beans, lima	25	50		
Beets (cooked)	55	100		
Cabbage (raw)	78	156		
Carrots (raw)	60	120		
Celery (raw)	100	200		
Corn, green, canned	25	50		
Cauliflower (raw)	80	160		
Dandelion greens	50	100		
Egg plant (cooked)	90	180		
Onions (boiled)	90	180		
Peas, green (cooked)	30	60	90	
Parsnips (raw)	40	80		
Potato (boiled)	25	50	75	

Fruits:

Apples (raw)	35	70		
Apricots (stewed)	40	80		
Bananas	25	50		
Blackberries (fresh)	35	70		
Cherries (fresh)	25	50		
Currants (fresh)	40	80		
Grape fruit	200			
Gooseberries	75	150		
Oranges	30	60		
Peaches	50	100		
Pears	40	80		
Plums	27	54		
Prunes (stewed)	25	50		
Raspberries	42	84		
Strawberries	60	120		

⁹ When no equivalent amount is mentioned in the third column, it is to be understood that the amount given in the second column is the maximum allowable.

TABLE D.

This table consists of a list of food materials which are not entirely free of sugars. They are allowed in quantities stated unless the patient is on a "carbohydrate-free" diet, when they must be avoided.

Vegetables (cooked without flour or sweetening): Dried peas and beans, either whole or in puree, turnips, carrots, salsify, green peas, lima beans, kidney beans, 2 tablespoonfuls.

Fresh Fruit: Apples, pears, apricots, peaches, 50 grams. Raspberries, strawberries, red currants, 1 large tablespoonful. Blackberries, 2 tablespoonfuls.

Stewed Fruit (with saccharine or crystallose): Plums, apples, pears, apricots, peaches, sour cherries, prunes, 1 heaped teaspoonful. Raspberries, gooseberries, red currants 2 heaped tablespoonfuls.

Dried Fruit: Plums, apricots, peaches, apples, prunes, 2 heaped tablespoonfuls.

Levulose chocolate (Stollwerck's) up to 15 grams.

Cocoa (without sugar) up to 12 grams.

HOW TO MAKE USE OF TABLE C.

The food is divided into two parts: (1) That which is free from carbohydrates, the principal fare, Tables A and B; and (2) that which contains carbohydrates, the secondary fare, Tables C and D. For instance, 75 grams of wheat bread are allowed in courses from Table C.

Breakfast: Principal fare, medium strong coffee or tea, cold meat, 1 egg and butter; secondary fare, 50 grams of oat cakes, the equivalent of which = 20 grams of wheat bread.

Second Breakfast: Two eggs in any form.

Dinner (mid-day meal): Principal fare, broth with egg, meat with green vegetables or salad (Table B), cheese and butter. Secondary fare, 50 grams of potatoes (= 20 grams of wheat bread), 60 grams of strawberries (= 10 grams of wheat bread).

Afternoon Meal: Tea, coffee, or consommé, with casoid cakes.

Supper: Principal fare, plenty of hot or cold meat, with vegetables or salad, cheese and butter; secondary fare, 25 grams of Graham bread (= 25 grams of wheat bread). Total, = 75 grams of wheat bread.

Oatmeal Diet. There is, at present, no scientific reason for the peculiar effect that oatmeal exercises on many diabetics; it is, however, true that in many cases in which large amounts of sugar are being excreted on a carbohydrate-poor diet, the institution of an exclusive oatmeal diet will result in the course of a few days in a sugar-free urine. This I have found most frequently in young diabetics, in whom the change effected by a week's treatment is sometimes wonderful, but it is in these very instances that one must not allow relatives of the patient to be deceived by the brightness of the outlook. The oatmeal diet is by all odds the best method of treating acidosis, and on this account it is not contraindicated in any type of case. Quite commonly with new cases in which there is some toxemia it is the best food to use for a few days, and leads the way to other methods. The chief obstacle that is encountered in the prolonged use of oatmeal is the intestinal derangements that ensue therefrom, taking the form of diarrhœa or severe constipation, and usually associated with marked tympanites. These symptoms are more prone to occur in children than with adults, but I have observed this only when the oat "cure" had been continued for over a week without intermission.

The most expedient mode of employing the oatmeal diet is as follows: An adult diabetic requires 16 calories of food value per pound body weight; if the patient weighs 150 pounds, he would need 2400 calories. Five ounces of butter—as much as can be

well taken—is equivalent to 1125 calories which leaves 1275 to be made up by the oatmeal. One ounce of dry oatmeal is equal to 113 calories, or 11 ounces to 1230 + calories. This amount (11 ounces) is weighed out and put into three pints of water, slightly salted, and thoroughly cooked for at least six hours; then while still hot it should be strained through a sieve. If the cooking is thoroughly done only the coarse covering of the kernel will remain on the sieve. The butter is added while the thick porridge is still hot and stirred into it. This is one day's food and may be taken, equal fractions—about seven ounces—every two hours or a larger allowance less frequently. No other food is to be permitted except a little black coffee or some brandy. This diet may be used three or four days at intervals without any hardship; longer periods require some fortitude on the part of the patient and firmness from the medical adviser.

Green Days. The object of the "green" or "vegetable" day is to decrease the food ingest, chiefly the protein factor. This is demanded in some cases because the ability to utilize carbohydrate is so slight that not even that resulting from the breaking down of the protein molecule is not burned. A "vegetable" day is then an attempt to put completely at rest a certain function, and in making up the dietary for such a routine the less protein entering into the food the better; of course, all carbohydrates are excluded. The bulk of food taken, therefore, is fat, and as this is of necessity small, a vegetable day amounts to the starvation days advised by Naunyn, with a thin disguise. The vegetables that may be used in this diet are any of the green variety that contain little or no carbohydrate other than cellulose (Table B); of these spinach, celery, cabbage, beet-tops, and the salads serve best. These may be varied to suit the taste of the patient.

The vegetable day might be ordered as follows:

Breakfast: A cup of coffee, a teaspoonful of cream, 3 egg yolks, served as omelet, with tomatoes and parsley.

Luncheon: 1 cup of bouillon; asparagus with egg sauce.

4 P.M.: A cup of coffee or a glass of wine with 1 casoid biscuit.

Dinner: A cup of bouillon; 1 box of sardines;¹⁰ spinach (boiled); 1 glass of wine or whisky.

Vegetable days are prone to increase markedly the formation of ketone bodies, and on this account, if the patient's urine shows the ferric chloride reaction before the diet is commenced, alkalis should be given during the vegetable day; 25 grams of a mixture of equal parts of sodium bicarbonate and citrate is usually sufficient. Vegetable days have their function in diminishing the sugar excretion, and in order completely to free the urine from sugar several vegetable days may be necessary.

¹⁰ The smoked Norwegian sardines are much more satisfactory than the other varieties on account of the flavor.

When this is the case, however, a most careful urine analysis is necessary daily to determine the degree of acidosis. When severe grades of ketonuria are caused by these "green days" it is best to follow them with one day of oatmeal. The number of days of each variety of diet (that is, vegetable days, "green days" and carbohydrate days), is a matter which must be determined by experiment with each individual.

Finally, it should be realized that the sugar output and acidosis are not the sole features on which success is to be judged. Patients must be frequently weighed and a constant loss of weight in a young person is quite as bad an omen as a large sugar output. Even with the most rigid diet regimen the nutrition should be maintained.

The dietary of the diabetic often seems to him extremely limited, and this can only be helped by variety in the manner of cooking foods. The receipts here appended are for the most part contributions from the families of patients.

SOUPS. *Consommé:* 3 pounds of beef from the round, 1 small knuckle of veal, 5 quarts of cold water—simmer four hours, then add: 1 pound each of carrots, turnips, and onions cut into dice, 1 teaspoonful of salt, $\frac{1}{2}$ teaspoonful of sweet marjoram, $\frac{1}{2}$ teaspoonful of thyme, 1 teaspoonful of peppercorns, 1 bay leaf, 1 sprig of parsley. Simmer one hour, strain and cool; when cold skim off the fat.

Consommé with Brussels Sprouts: To three pints of hot consommé add 2 cupfuls of Brussels sprouts which have been soaked in cold water twenty minutes, and boiled in boiling salted water fifteen minutes.

Consommé with Claret: To 1 pint of consommé add 1 pint of claret, 1 pint of hot water, pour 1 cupful of consommé over the yolks of 3 eggs; cook until the spoon is coated; add the beaten egg whites. Mix and serve either hot or cold.

Consommé with Cucumbers: To 3 pints of consommé add 2 sliced cucumbers which have been cooked one-half hour in 1 cupful of water. For the cucumbers may be substituted, red or white cabbage, cauliflower, asparagus, cooked meats chopped, or Parmesan cheese.

Tomato Soup: Stew tomatoes with butter, strain, and add an equal quantity of consommé.

Jacobin Cubes: Beat 3 eggs in a bowl, add some nutmeg and 3 teaspoonfuls of water; place the bowl in boiling water until the mixture thickens; cut in cubes and serve in broth.

For pureés, rub through a sieve cooked cauliflower, asparagus, or tomatoes; add to 3 pints of hot consommé and pour over 1 cupful of cream in which 2 egg yolks have been stirred.

SAUCES. *Cucumber Sauce:* Cut up 2 cucumbers in cubes after removing the seeds, stew them in 1 cupful of sour cream until

soft. Stir up 1 egg yolk with 1 cupful of cream in a double boiler until it thickens; add this to the cucumbers and heat again; season with salt and pepper.

Sauce Tartare: Slowly stir 1 egg yolk adding $\frac{1}{2}$ cupful of olive oil, drop by drop, 2 tablespoonfuls of vinegar, also by drops, salt, pepper, 1 teaspoonful of French mustard and a little parsley. Stir on ice.

Mustard Sauce: 1 pound of melted butter, 1 pound of French mustard covered with broth, $\frac{1}{4}$ teaspoonful of salt, 1 teaspoonful of vinegar, take off the fire and beat in 1 yolk.

Horseradish Sauce: Stir a piece of butter with 2 tablespoonfuls of grated horseradish, add pepper and salt, cover with broth, and boil for one-half hour.

Brown Onion Sauce: 2 onions chopped and stewed in butter until brown, covered with broth, 1 teaspoonful vinegar, pepper, a clove, a bay leaf, a slice of lemon.

Sauce Bearnaise: Cook in double boiler, stirring constantly, 3 egg yolks, 1 teaspoonful of water, 1 teaspoonful of butter; add one at a time, 4 tablespoonfuls of butter; stir until boiling, and add 1 teaspoonful each of tarragon, or plain vinegar, tarragon leaves, and parsley minced.

Tomato Sauce: Tomatoes after being passed through a sieve are stewed in butter and covered with broth.

Mushroom Sauce: Mushrooms are stewed in butter and covered with broth or gravy. Take off the fire and beat in 1 yolk.

White sauce for asparagus, artichokes, etc.: Mix 1 tablespoonful of butter, 2 yolks, and 1 cupful of cream, cold; cook in a double boiler, beat constantly until thick. Serve immediately.

Spinach Pudding: Mix with 1 quart of boiled spinach 4 yolks, add $\frac{1}{2}$ onion, $\frac{1}{2}$ cupful of cream, whites whipped stiff, and $\frac{1}{2}$ cupful of ham cut in cubes. Place the mixture in a well-buttered dish and steam in a "bain Marie."

Baked Cauliflower: Place soft boiled cauliflower in an open pie dish, pour sour cream, melted butter, and parmesan cheese over it; then bake in the oven.

Tomato Jelly Salad: To one can of stewed and strained tomatoes, add 1 teaspoonful of salt and $\frac{2}{3}$ box of gelatin soaked and dissolved. Pour into small cups and chill. Serve on lettuce leaves with mayonnaise dressing.

Oatmeal Muffins: To 2 half-pint-cupfuls of finely ground (coffee grinder) oatmeal add 1 heaped teaspoonful of Royal baking powder and $\frac{1}{2}$ teaspoonful of salt. Mix well, add $1\frac{1}{2}$ cupfuls of cold water, and at last a piece of melted butter (or lard) the size of an egg. Beat well for a minute, put in muffin tins, and bake in a hot oven.

Coffee Mousse: 1 quart of thin cream; 1 cupful of strong coffee; $1\frac{1}{4}$ tablespoonfuls of granular gelatine; 2 tablespoonfuls of cold

water; 3 tablespoonfuls of hot water, and saccharine to taste. Add the gelatine soaked in cold water and dissolved in boiling water to the coffee. Set the mixture in a pan of ice water and stir until it begins to thicken; then fold in whipped cream, put in mold cover, pack in equal parts of salt and ice, and let stand four hours.

Stuffed Eggs: Mash up the yolks of 5 hard-boiled eggs with a lump of butter, thicken with parmesan cheese, 1 raw egg, and some sour cream. Fill the whites of the 5 eggs, tops and bottom with this mixture, place in a buttered tin, sprinkle with cream and cheese, and bake in the oven.

Ragout Eggs: Mash the yolks of 6 hard-boiled eggs with a fork, slice 2 onions and stew them in 2 tablespoonfuls of butter until they are soft without allowing them to brown. Add the yolks with salt, pepper, marjoram, and nutmeg, and stir in a cupful of sweet cream. Garnish the dish with the whites quartered.

Lemon Soufflé: Stir 4 yolks until they thicken, sweeten with saccharin, add the juice of half a lemon, some lemon rind grated, and 4 whites whipped stiff. Bake for ten minutes.

Wind Puffs: For 2 wind puffs stir 4 whole eggs, 2 tablespoonfuls of sweet cream, a pinch of salt, and a little saccharin, well for half an hour until the mixture is turned into a stiff froth. Pour into two buttered tins and bake in a hot oven for about half an hour. Serve hot with whipped cream.

Fish Scallops: 1 cupful of cooked fish freed from bone. Mix with 1 egg, capers, parmesan cheese, salt, and sour cream. Butter the scallops, fill in the mixture, sprinkle with powdered parmesan cheese, and bake in oven.

Cheese Soufflé: Grate 4 ounces of parmesan and $2\frac{1}{2}$ ounces of Swiss cheese. Stir well with $4\frac{2}{3}$ ounces of fresh melted butter, the yolks of 8 or 10 eggs and the whites beaten stiff. Season with ground white pepper and salt. Fill two small porcelain moulds, bake slowly for from ten to fifteen minutes, then serve quickly.

Cabbage Soufflé: Boil white cabbage in salt water. Chop fine, then stew with an onion and 1 pound of minced pork. Beat up 2 eggs with 6 or 8 spoonfuls of sour cream; whip 2 whites of egg; then stir the whole into the cabbage. Fill a buttered tin, sprinkle with parmesan cheese, and bake in the oven for one hour. Serve with tomato sauce.

Coffee or Orange Charlotte: $\frac{1}{2}$ box of gelatin; $\frac{1}{2}$ cupful of cold water; $\frac{1}{2}$ cupful of boiling water; 3 tablespoonfuls of lemon juice; 1 cupful of orange juice and pulp or 1 cupful of coffee; and the whites of 3 eggs. Whip from 2 cupfuls of cream, saccharin to taste. Soak the gelatin in cold water and dissolve in boiling water; strain, and add to juice or coffee; chill the mixture in a pan of ice water; when quite thick beat with wire whisk until frothy, then add the whites of the eggs beaten stiff, and fold in cream. Turn into wet mould and chill.

Spanish Cream: $\frac{1}{4}$ box of gelatin; $\frac{1}{4}$ cupful of cold water; $\frac{3}{4}$ cupful boiling water; 3 eggs; $\frac{1}{2}$ teaspoonful of salt; 1 pint of milk; vanilla, 1 teaspoonful; and saccharin to taste. Soak the gelatin in cold water, dissolve in boiling water. Make a custard with the yolks of the eggs beaten, and mixed with salt. Pour on the hot milk, and cook in double boiler until it thickens. Add the strained gelatin water, vanilla, saccharin, and the whites of the eggs beaten stiff. Mix well and turn into a mold wet in cold water. Place on ice until hard.

Boiled Custard: The yolks of 3 eggs; $\frac{1}{2}$ teaspoonful of salt; 1 pint of hot milk; $\frac{1}{2}$ teaspoonful of vanilla; and saccharin to taste. Scald the milk. Beat the yolks, add the salt, and the saccharin, and pour the hot milk slowly into the eggs; when well mixed, pour all back into the double boiler, and stir constantly until smooth and thick like cream; strain when cool, and add vanilla.

Snow Pudding: $\frac{1}{4}$ box of gelatin; $\frac{1}{4}$ cupful of cold water; 1 cupful of boiling water; $\frac{1}{4}$ cupful of lemon juice; the whites of 3 eggs, and saccharin to taste. Soak the gelatin in cold water, dissolve in boiling water, strain, add the lemon juice and saccharin, and set in ice water to cool. Stir occasionally. Beat the whites of the eggs to a stiff froth, and when the gelatin begins to thicken add the beaten whites and beat all together until very light; chill in a wet mould. Serve with boiled custard.

Coffee Jelly: $\frac{1}{2}$ box of gelatin; $\frac{1}{2}$ cupful of cold water; 1 cupful of boiling water; 3 cupfuls of coffee, and saccharin to taste. Soak the gelatin in cold water, dissolve in boiling water, and strain into sweetened coffee; pour into a wet mould and chill until firm. Serve with whipped cream.

Baked Custard: 1 quart of milk; 6 eggs; 1 teaspoonful of salt, and saccharin. Scald the milk. Beat the eggs, add the salt, and sweeten; then add the scalded milk. Strain, add a little nutmeg, and bake about twenty minutes in a dish set in a pan of warm water or in custard cups set in water.

Almond Cake: Beat $\frac{1}{2}$ pound of butter and 8 egg-yolks vigorously for one-quarter hour. Mix 20 grams of baking powder, 100 grams of plasmon, lemon rind grated and the juice of 1 lemon, 1 teaspoonful of vanilla, and $\frac{1}{4}$ pound of finely chopped almonds, and add to the beaten yolks. Sweeten with saccharin, and lastly fold the 8 whites into the mixture and bake in well-buttered tin for one-half hour.

Chocolate Sauce: 1 tablespoonful of diabetic chocolate in a double boiler with $\frac{1}{2}$ pint of milk, and 3 egg-yolks. Stir until it begins to thicken. When cold, add a pint of whipped cream.

Pudding a la Nesselrode: Stir 5 yolks over the fire with a little water until they thicken, add 7 ounces of finely chopped almonds, 3 tablespoonfuls of cognac, 1 tablespoonful of dissolved gelatin, and 15 whites whipped stiff. Fill into a mould rinsed with water.

A RESUME OF VACCINE THERAPY.

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IN reviewing the work of various authorities with vaccine therapy, no claim is made that the statements given by them are correct in every detail, and the reader is cautioned to make allowance for the many factors that might have influenced the apparent results obtained. Among these may be mentioned: the overzealousness that often exists in taking up a new work or in trying a new remedy which may sometimes eclipse the better judgment of an observer; the part that nature plays in effecting a spontaneous cure in a given case may be overlooked, or the results obtained when viewed through the eyes of a less enthusiastic and more stoical observer might present a different picture. There is also the question whether the cases under consideration were mild or severe in character or whether they were typical cases. It must also be remembered that a large number of sporadic cases in which brilliant results have been obtained are reported, while probably a larger number of cases that have been unsuccessfully treated are not reported.

It is realized that statistics at best are not always reliable, and perhaps, when it is impossible to make comparisons with other modes of treatment, they are undesirable; however, when the results obtained by a number of observers closely coincide, it is only fair to conclude that such results indicate the value or uselessness of the method of treatment under consideration.

In order to arrive at a definite conclusion as to the value of a method of treatment of a given disease, it is desirable to consider as large a number of cases as possible; and, while the medical literature abounds in articles on vaccine therapy, they are scattered through a large number of medical journals, covering several years. It is with the hope that by grouping together the cases from the literature that the reader may at a glance gain a better comprehension of the work being done and the results accomplished in this line, that this paper has been written.

Assuming that the majority of readers will be more interested in the results accomplished in specific conditions, a classification has been made according to diseases instead of the more scientific method usually employed in articles of this nature, in which the classification is made according to the specific organism.

GENERAL INFECTIONS.

Actinomycosis.

Wynn¹⁵² has successfully treated a case of actinomycosis of the lung with a vaccine made from a culture of *Streptothrix bovis*.

The first inoculation resulted in a marked diminution of the purulent discharge; the temperature dropped to normal, and continued so for three days, after which there was a slight rise. After the second injection, however, it again became normal, and remained so. Six injections were given during eleven weeks, at the end of which time the patient was discharged cured. One year after inoculation the patient was still in good health.

Bubonic Plague.

Bacterial vaccines have been used a number of years in the prophylactic treatment of bubonic plague by Haffkine,⁵¹ with marked success. He states that of 639,630 persons in whom the vaccine had not been used, 49,433, or 7.7 per cent., developed the disease, and 29,733, or 4.7 per cent., died; whereas, of 186,797 who had been inoculated with plague vaccine, only 3399, or 0.8 per cent., developed the disease, with 814, or 0.4 per cent., deaths. Haffkine is under the impression that early use of the vaccine may abort the disease.

Cholera.

Haffkine⁵⁰ has also used bacterial vaccines in the prophylaxis of Asiatic cholera with success. He states that about ten times the number of those not inoculated are attacked to those that are inoculated. Powell¹⁰¹ has collected the following statistics:

Of 6549 that did not receive the inoculations, 198, or 3 per cent., developed the disease, and 124, or 1.8 per cent., died; of 5778 that had received the inoculations, only 27, or 0.46 per cent., were attacked, and 14, or 0.24 per cent., died. The vaccine does no good when the disease is once contracted. The immunization lasts about fourteen months.

Glanders.

Two cases of glanders treated with bacterial vaccines by which cures were effected have been reported, one by Bristow and White,¹⁸ and the other by Zieler.¹⁵³ Both were general infections.

Pyemia.

Authors.	Cases.	Cured.	Improved.	Remarks.
Floyd ⁴¹	1	0	0	Not benefited.
Crofton ³³	1	1	0	
Oastler ⁹⁶	1	0	1	
Grove ⁴⁹	1	1	0	
Harris ⁵⁵	1	1	0	One not benefited.
Thompson ¹²⁹	1	1	0	
Hoobler ⁶³	2	2	0	
McDonald ⁸³	5	4	0	
Oastler ⁹⁷	1	1	0	
	<hr/>	<hr/>	<hr/>	
	14	11	1	2 not benefited.

In pyemia, the inoculation treatment seems to have met with general success, although the number of cases in this series is rather small to form any definite opinion.

Scarlet Fever.

Smith¹²⁵ has collected from the literature 4771 preventive inoculations against scarlet fever with a vaccine made from a bouillon culture of a streptococcus isolated from a person ill with scarlet fever and killed by heating to 60° C., according to the method described by Gabritschewsky.⁴³ These vaccines were used by physicians in epidemics of scarlet fever occurring in Russian villages in which 15 per cent. to 70 per cent. of the uninoculated were stricken with the disease. Of those that had received three doses of the vaccine, none were effected; of 2034 that had received two or more vaccinations, only 2 were attacked; of 2737 others who had received only one dose of the vaccines, 41 were attacked. Most of the cases that had received vaccine treatment ran an exceedingly mild course. Three injections of the vaccine is supposed to confer immunity for about one and one-half years.

Septicemia.

Unclassified.

Authors.	Cases.	Cured.	Improved.	Remarks.
Boellke ¹³	1	1	0	
Harris ¹⁶	2	2	0	
Hartwell ⁶⁰	9	0	5	Four not benefited.
White and Eyre ¹⁴²	1	1	0	
Allen ²	2	2	0	
McDonald ⁸³	7	3	0	Four not benefited.
Floyd ⁴¹	1	1	0	
Turton ¹³³	1	1	0	

Gonococcic.

Eyre ³³	1	0	1	
Dieulafoy ³⁶	2	2	0	
Irons ⁶³	3	0	0	Not benefited.
Miller ⁹²	1	1	0	

Puerperal.

Lloyd ⁷³	2	0	2	
Floyd ⁴¹	1	1	0	
Riebardson ¹⁰³	2	1	0	One not benefited.
Bristow ¹⁶	2	2	0	
Martyn ⁹⁹	1	1	0	
Crowe ³⁴	1	1	0	
Turton ¹³³	3	1	1	One not benefited.
Strubell ¹²⁷	1	0	1	
Oastler ⁹⁶	2	1	0	One not benefited.
Leary ⁷⁷	47	43	0	Four not benefited.
White ¹⁴²	1	0	0	Not benefited.
Hartwell ⁶⁰	18	18	0	
Hoobler ⁶³	3	3	0	
Oastler ⁹⁷	2	1	0	One not benefited.
Sherman ¹²⁹	1	1	0	
	118	88	10	20 not benefited.

Of the cases of septicemia that have not been classified, 8 were due to the streptococcus, 4 to the pneumococcus, 1 to Friedländer's bacillus, 1 to the colon bacillus, and 1 was a mixed streptococcic and staphylococcic infection, and in the others, the causative organism was not given. Of the cases not benefited by vaccine therapy, 4 were due to the streptococcus and 4 were cases of which the organism was not given.

The results obtained by vaccine therapy in the treatment of puerperal septicemia are particularly gratifying, especially in the 18 cases reported by Hartwell, Streeter, and Green, in which every case recovered. No less remarkable is the series of 47 cases treated by Leary, in which there were only four deaths. Leary states that in most of these cases vaccine therapy was only used as a last resort, and 2 of the cases were moribund when treatment was begun. Martyn's case had received three doses of antistreptococcic serum without the slightest effect before vaccine treatment was adopted, after which improvement took place rapidly.

TYPHOID FEVER.

Prophylactic Inoculations.

		Cases of typhoid.	Cases per 10,000	Deaths of typhoid.	Deaths per 10,000.
McRae, ⁸⁴ Boer War (1899 to 1902):					
Not inoculated	150,231	3739	242	257	17.1
Inoculated	19,069	226	118	39	20.0
Kuhn, ⁴⁷ German South African Troops (1902-1906):					
Not inoculated	9209	906	980	116	120.0
Inoculated	7287	371	500	24	33.0
Leischman, ⁷⁸ British Colonial Army (to June, 1908):					
Not inoculated	6610	187	283	26	39.3
Inoculated	5473	21	38	2	3.6

The earlier prophylactic inoculations against typhoid fever do not present anything very striking; indeed, while the incidence of attack seems to be reduced, the death rate is slightly higher. However, the inoculation of the German South African troops gave better results, and Leischman's report of the British Colonial Army are very encouraging. Russell¹¹³ has inoculated 1400 American soldiers, and Hartsock⁵⁰ 563. It is too early to learn anything of the results of these inoculations as yet.

Typhoid Fever.

Authors.	Cases.	Results.
Richardson, ¹⁰⁰	40	5 per cent. relapsed; 163 cases not inoculated, 21.4 per cent. relapsed.
Illman ⁶⁶	1	Not benefited.
Watters ¹³⁸	30	Had mild course. One case not benefited.
Watters ¹³⁹	4	Had mild course.
Smallman ¹²³	36	Generally a mild course. Three deaths.
Semple ¹¹⁹	9	Generally a mild and short course. All recovered.
Nichols ⁹⁵	11	Generally mild; no deaths; 2 relapses.
Richardson ¹⁰¹	28	Only one relapsed.
Raw ¹⁰²	9	No marked effect; 2 died.

Carrier Cases.

Irwin & Houston ⁶⁹	1	Cured.
Houston ⁶⁵	3	Two cured; one markedly improved.

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The treatment of typhoid fever by bacterial vaccines has not met with very marked success as yet, and the results claimed by various authors are at variance. Richardson has not noted any marked improvement due to the treatment, but thinks that relapses are largely prevented. Other observers do not note this fact, but are of the opinion that when treated with vaccines the disease has a much milder course. In the 34 cases treated by Watters and Eaton, the temperature became normal in 1 case on the eighth day, in 1 on the eleventh, 1 on the twelfth, 1 on the fourteenth, 2 on the sixteenth, 2 on the seventeenth, 3 on the eighteenth, 1 on the twentieth, 2 on the twenty-first, 4 on the twenty-second, 1 on the twenty-fourth, 1 on the twenty-sixth, 1 on the twenty-seventh, and 2 on the twenty-eighth day of the disease. Two of the cases that reached normal on the seventeenth day had relapses, and one of the cases did not respond to treatment at all. These authors compare the death rate of 31 cases treated with vaccines to that of 46 other cases that received routine treatment only. In the former the death rate was 3.2 per cent., while in the latter it was 11.1 per cent. Two of the cases treated by Semple with autogenous vaccines had normal temperatures on the eighteenth and nineteenth days, respectively.

In the treatment of carrier cases of typhoid fever, vaccine therapy may prove of untold value, if further investigations give results similar to the ones tabulated. The case reported by Irwin and Houston occurred in a domestic who had had typhoid fever seven years previously. In the interval six people in families in which she worked contracted typhoid fever. An examination of her stools and urine revealed the presence of many typhoid bacilli in the latter. She was treated with urinary antiseptics, tonics, and rest for five weeks, at the end of which time the bacilli were still present in the urine. An autogenous vaccine was prepared, and after the fourth injection the organisms disappeared from the urine. Three subsequent examinations of the stools and urine were negative, and a marked improvement in the general health of the patient resulted.

DISEASES OF THE DIGESTIVE TRACT.

Pyorrhœa Alveolaris.

Authors.	Cases.	Cured.	Improved.	Remarks.
Carmalt-Jones ²⁵	5	2	1	One not benefited.
Goadby ⁴⁸	2	2	0	
Beebe ⁶	17	6	11	
Goadby ⁴⁵	51	36	9	Four not benefited.
Fisher ³⁹	1	0	1	
	<hr/> 76	<hr/> 46	<hr/> 22	5 not benefited.

One of the cases of Carmalt-Jones and Humphreys discontinued treatment, and 2 of Goadby's cases died of intercurrent diseases.

Cancrum Oris.

Mallanah⁸⁸ reports a case of cancrum oris from which *Staphylococcus aureus* was isolated. A vaccine was administered and a cure resulted.

Cholecystitis.

Wright and Reid¹⁵⁰ report 2 cases of cholecystitis treated with vaccines, both of which were cured. One case was that of obstructed jaundice, which was not relieved by operation, and the bile was discharged through a sinus. *Bacillus coli* was isolated from the bile, a vaccine prepared, and after three injections the sinus closed and the jaundice cleared up, resulting in a complete cure. The second case was one in which fourteen stones had been removed from the gall-bladder two months previously; the sinus remained open and the patient did not improve. Under vaccine treatment the sinus closed and the patient made a somewhat slow but complete recovery.

In a case reported by Turton and Parkin,¹³⁴ the patient had been ill three weeks with gradual loss of flesh, abdominal pain, rigors, and at intervals swelling of the epigastrium. He was operated on for pancreatic disease, but the pancreas was found to be normal and a large stone was removed from the gall-bladder. The rigors continued, and the patient was sent home to die. Examination of the gall-bladder secretions gave a pure culture of *Bacillus coli*. A vaccine was made and 500,000,000 inoculated. This was followed by one rigor three days after the inoculation. Two more injections were given, and the patient made a rapid and complete recovery.

Ulcerative Colitis.

White and Eyre¹⁴² report 3 cases of ulcerative colitis treated with a vaccine made from the colon bacillus, which had been isolated from the intestine. All three cases were cured.

Tuberculous Enteritis.

Turton and Parkin¹³¹ treated 2 cases of tuberculous enteritis with tuberculin, both cases showing marked improvement. One case of tuberculous enteritis treated by Thomas¹²⁸ died.

Gastritis.

White and Eyre¹⁴² report a case of gastritis occurring in a female, aged thirty-six years, who for over eight months had had nausea, heartburn, chilliness, slight rise in temperature, and who had a severe feeling of illness and was completely incapacitated. During the attacks she was constipated and had lost much flesh. Different physicians had diagnosed duodenal ulcer and atonic dilatation of the stomach. Stomach washings contained many colon bacilli, from which a vaccine was prepared and administered. After the first injection the patient showed improvement, and after five months' treatment she had gained fifteen and one-half pounds in weight; her appetite was good, and she felt perfectly well. When seen seven months later she was doing well and had no further attacks.

Peritonitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Turton ¹³¹	1	1	0	
Beebe ⁷	1	1	0	
Illman ⁶⁶	2	1	0	One not benefited.
Robinson ¹¹⁷	1	1	0	
Wolfsohn ¹⁴⁵	1	0	1	
Fisher ³³	1	0	0	One not benefited.
	<hr/> 7	<hr/> 4	<hr/> 1	<hr/> 2 not benefited.

The cases reported by Illman and Duncan and by Wolfsohn were tuberculous peritonitis. Those reported by Beebe and Medalia, Turton and Parkin, and Fisher, were due to the colon bacillus, and the case of Robinson was due to the pneumococcus.

Gonorrhæal Proctitis.

Illman and Duncan⁶⁶ report a case of gonorrhæal proctitis successfully treated with gonococcic vaccine.

DISEASES OF THE RESPIRATORY SYSTEM.

Bronchiectasis.

McDonald⁸³ reports 3 cases of bronchiectasis treated with vaccines, one of which was cured. The other two were not benefited.

Bronchial Asthma.

Authors.	Cases.	Cured.	Improved.	
Briscoe ¹⁴	1	1	0	
Harris ⁵⁵	1	0	1	
Allen ²	1	1	0	
Carmalt Jones ²⁴	52	0	48	Four not benefited.
Fisher ³³	1	1	0	
	<hr/> 56	<hr/> 3	<hr/> 49	4 not benefited.

The vaccine used by Carmalt-Jones was made from an unknown organism isolated from a case of bronchial asthma. Thirty-one of these cases have found some degree of improvement in the frequency, and 39 in the severity of the attacks; 26 have improved in their power of taking exercise, and 29 have slept better. The cases of Briscoe and Williams and of Fisher were treated with a vaccine made from the staphylococcus and influenza bacillus; that of Harris by a vaccine made from *Micrococcus catarrhalis* and the pneumococcus; and that of Allen by a mixed vaccine.

Pneumonia.

Authors.	Cases.	Results.
Wolf ¹⁴⁵	14	Eleven recovered; 40 per cent. of deaths in untreated.
Boellke ¹³	13	All cured; three days average duration after inoculation.
Leary ⁷⁷	83	Seventy-one recovered.
Batten ⁵	1	Cured.
Harris ⁵⁵	7	Four had crisis on average twelve hours; three not benefited.
Allen ²	1	Delayed resolution. Cured.
Willcox ¹⁴⁴	24	Twenty-three cured.
Graig ³²	6	All cured.
Fisher ³³	6	Five cured.
	<hr/> 155	<hr/> 135 recovered.

MacDonald,⁸⁶ working in the bacteriological department of the London Hospital, laid the foundation for the vaccine treatment of pneumonia by producing artificial crises in rabbits infected with the pneumococcus. These infected animals were inoculated with a vaccine made from the same strain with which they had been infected, and he was able to produce a crisis and recovery at will. Rabbits used as controls on which the vaccines were not used, died.

The death rate from pneumonia varies under different conditions, and is estimated at from 25 per cent. to 60 per cent. In an analysis of 43,455 cases, Musser and Norris⁸⁴ found an average mortality of 21.06 per cent. The average mortality in this series of 155 cases is 12.9 per cent.

In the 14 cases treated by Wolf, the death rate was 27.2 per cent., while in other cases of the same epidemic that did not receive vaccine treatment, the death rate was 40 per cent. The crisis occurred in thirty-six hours after inoculation in ten of the eleven patients that recovered.

In Leary's 83 cases, 34 occurred in alcoholics, a class of patients in which the death rate in pneumonia is unusually high, averaging about 50 per cent. Of these 34 cases, 6 died, a mortality of 17.7 per cent. Of the other 49 cases, only 2 died, a death rate of 4.08 per cent., or a total mortality for the entire series of 83 cases of 9.7 per cent.

Of particular interest is the series of cases treated by Craig. These 6 cases occurred in the Sailor's Snug Harbor Hospital, New Brighton, where the inmates are all over sixty years of age, and where the mortality rate from pneumonia has averaged 66.6 per cent. during the past four years. The patients were aged sixty-six years, sixty-seven, seventy-three, seventy-five years and five months, eighty, and eighty-three years old, respectively. Three of the patients were alcoholics, and 2 of the cases followed an alcoholic debauch. Five had chronic nephritis, and all had marked arteriosclerosis. All the cases were treated with vaccines, and all recovered.

Empyema.

Authors	Cases.	Cured.	Improved.	Remarks.
Lyon ⁸¹	1	1	0	
Ohlmacher ⁷⁹	1	1	0	
Ross ¹¹¹	1	1	0	
Ross ¹¹⁰	1	1	0	
Boellke ¹³	1	1	0	
Western ¹⁴¹	2	2	0	
Briseoe ¹⁴	2	0	1	One not benefited.
Floyd ⁴¹	3	3	0	
Beebe ⁷	3	1	2	
Harris ⁵⁵	1	1	0	
White ¹⁴²	3	2	0	One not benefited.
Hartwell ⁶⁰	6	0	0	Not much benefited.
Hoobler ⁶²	1	1	0	
Thomas ¹²³	2	1	1	
	<hr/> 28	<hr/> 16	<hr/> 4	<hr/> 8 not benefited.

A large number of this series were cases in which the condition and persisted for some time, with little or no improvement, and vaccine therapy was only administered as a last resort. The case of Lyon is worthy of note, because of the almost remarkable results achieved. Resection of the rib was followed by a chronic discharge of about half an ounce of pus daily, which continued without any signs of improvement for nine weeks. At this time an autogenous pneumococcic vaccine was administered; the patient began to improve at once, and fourteen days after the first inoculation was able to return to work.

DISEASES OF THE CIRCULATORY SYSTEM.

Acute Ulcerative Endocarditis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Barr ⁴	1	1	0	
Wright ¹⁴⁹	6	2	1	Three not benefited.
Ross ¹¹¹	1	1	0	
Western ¹⁴¹	2	0	0	Not benefited.
Boellke ¹³	1	1	0	
Horder ⁶⁴	4	2	0	Two not benefited.
Ladd ⁷⁵	2	0	2	
Conders ³¹	1	1	0	
Thompson ¹²⁹	7	3	4	
Hoobler ⁴³	1	0	1	
	<hr/> 26	<hr/> 11	<hr/> 8	<hr/> 7 not benefited.

Of the above series of 26 cases, 22 were due to the streptococcus, 2 were due to the pneumococcus, and 2 were due to the influenza bacillus. The case reported by Barr, Bell, and Douglas had received five doses of antistreptococcic serum without effect. On the thirty-ninth day of the disease the patient received an autogenous streptococcic vaccine, and marked improvement followed immediately. Thompson states that in his 7 cases the administration of an autogenous vaccine never failed to produce some improvement, such as a fall in temperature or other indication of benefit

DISEASES OF THE DUCTLESS GLANDS.

Adenitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Ohlmacher ⁹⁹	1	1	0	
Strubell ¹²³	1	0	0	Not benefited.
Sherman ¹²⁰	1	1	0	

Tuberculous.

Turton ¹³¹	8	1	6	One not benefited.
Ross ¹¹⁰	2	1	1	
Painter ¹⁰⁰	2	0	0	Not benefited.
McArthurs ⁸²	2	0	2	
Ross ¹¹¹	2	2	0	
Western ¹⁴¹	5	4	0	One not benefited.
Beebe ⁷	4	2	2	
Illman ⁶⁶	2	2	0	
Grant ⁴⁸	1	1	0	
Turton ¹³³	10	8	2	
Carmalt ²³	79	27	30	Twelve not benefited.
Miller ⁹²	2	1	1	
	<hr/> 122	<hr/> 51	<hr/> 44	<hr/> 17 not benefited.

The cases of acute adenitis are too few to form any judgment as to the value of vaccine treatment in this condition. Tuberculous

adenitis is usually benefited by the administration of tuberculin, and many surgical operations are rendered unnecessary. This is especially true of those cases treated before caseation occurs, in which, as a rule, a cure is effected. Caseated masses and abscesses should be treated both surgically and by vaccines. When sinuses have formed, mixed vaccines should be employed.

DISEASES OF THE GENITO-URINARY SYSTEM.

Acute Nephritis.

White and Eyre¹⁴² report a case of acute nephritis which was treated with a mixed *Staphylococcus aureus* and *Bacillus colon* vaccine with success.

Tuberculosis of the Kidney.

Authors.	Cases.	Cured.	Improved.	Remarks.
Turton ¹³⁴	2	0	2	
McArthurs ⁵²	2	2	0	
Walker ¹³⁷	1	0	1	
Turton ¹³⁵	4	0	3	One not benefited.
Carmalt-Jones ⁵³	8	2	5	One not benefited.
Miller ⁵²	2	1	1	
	19	5	12	2 not benefited.

The results obtained in tuberculosis of the kidney are encouraging, and it would seem that at least tuberculin should be employed in those cases in which, for any reason, operation is contraindicated, or in the cases that refuse operation.

Pyelonephritis.

Routh¹⁴⁴ reports a case of pyelonephritis of pregnancy from which the colon bacillus was isolated. A vaccine was made and administered, and a cure resulted. Hartwell and Streeter⁵⁰ also report a case of pyelonephritis treated with a colon vaccine with improvement.

Pyelitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Hicks ⁵¹	1	1	0	
White ¹⁴²	2	1	0	One not benefited.
Cunningham ⁵⁵	2	1	1	
Hartwell ⁵⁰	6	2	2	Two not benefited.
Fisher ⁵²	1	1	0	
Billings ¹³	2	2	0	
	14	8	3	3 not benefited.

All of the above 14 cases were due to the colon bacillus except 1 of the 2 cases reported by Cunningham, which was a mixed colon and tuberculous infection. This case was improved.

*Cystitis.**Unclassified*

Authors.	Cases.	Cured.	Improved.	Remarks.
Floyd ⁴¹	1	1	0	Uro-bacillus infection.
Miller ⁹¹	1	1	1	Friedlander's bac. infection.
Wolfsohn ¹	1	0	1	Bacillus fluorescens infection.
Hartwell ⁵⁹	6	4	0	Mixed infections. Two not benefited.

Tuberculous Infections.

Ohlmacher ⁹⁹	1	0	1	
Ross ¹¹⁰	1	1	0	
Ross ¹¹¹	1	1	0	
Walker ¹³⁷	1	1	0	
Carmalt-Jones ¹³	17	2	12	Three not benefited.

Colon Infections.

Ohlmacher ⁹⁹	1	1	0	
Western ¹⁴¹	2	1	1	
Rodd ¹⁰⁸	2	1	1	
McArthur ⁸²	2	0	2	
Floyd ⁴¹	2	2	0	
Beebe ⁷	3	1	2	
Illman ⁹⁶	1	1	0	
Clark ²⁸	1	1	0	
Turton ¹³³	1	1	0	
White ¹⁴²	5	4	0	One not benefited
Thomas ¹²³	1	0	1	
Wulff ¹⁵¹	21	18	0	Three not much improved.
Hartwell ⁵⁹	5	1	4	
McDonald ³³	4	3	0	One not benefited.
Billings ¹²	2	2	0	
	<hr/> 83	<hr/> 47	<hr/> 26	<hr/> 10 not benefited.

The results in the treatment of cystitis with vaccine are very good, especially the colon infections, in which the good effects are usually early apparent and well marked, frequent urination and pain disappearing quickly. The complete disappearance of the organisms from the urine, however, often requires rather long treatment.

Urethrocystitis.

Ballenger³ reports 3 cases of gonorrhoeal urethrocystitis treated with gonococcic vaccine with much benefit.

Epididymitis.

Authors.	Cases.	Cured.	Improved.	Remarks
Ohlmacher ⁹⁹	2	1	1	
Ballenger ³	2	0	2	
Jamieson ⁷²	1	1	0	
Walker ¹³⁷	1	0	1	
	<hr/> 6	<hr/> 2	<hr/> 4	

The case reported by Walker was tuberculous epididymitis. The other 5 cases were due to the gonococcus. The number of cases is

too few to form any opinion of the value of vaccines in these conditions, but Belfield,¹⁰ while not citing any cases in summing up the treatment of "Pus Tubes in the Male," states: "Vaccine therapy, accurately applied, is the most valuable internal measure against the infections which produce pus tubes in the male."

Orchitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Eyre ³³	3	3	0	
Wolfsohn ¹⁴⁰	1	1	0	
Carmalt-Jones ²³	8	3	4	One not benefited.
	<hr/> 12	<hr/> 7	<hr/> 4	1 not benefited.

The 3 cases reported by Eyre and Stewart were due to the gonococcus. The remaining 9 cases were tuberculous.

Prostatitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Bellenger ³	10	0	10	
Robertson ¹⁰⁶	6	6	0	
Rooker ¹⁰⁹	1	1	0	
Thomas ¹²³	1	0	1	
	<hr/> 18	<hr/> 7	<hr/> 11	

Four of the cases of the above series were acute, and the remaining cases were chronic prostatitis. Of the acute cases, 1 was cured and the remainder benefited by the use of vaccines. Six of the chronic cases were cured and the remaining 8 were improved. The acute case reported by Rooker was due to *Staphylococcus aureus*, and was cured by the use of a vaccine made from this organism. The remaining 17 cases were gonorrhœal. The 6 cases reported by Robertson were chronic cases following gonorrhœa. They were not relieved by routine treatment nor by the inoculation of gonococcic vaccines. The injection of a vaccine made from *Staphylococcus albus* resulted in a cure of all of the cases.

Urethritis (Gonorrhœal).

<i>Acute.</i>				
Authors.	Cases.	Cured.	Improved.	Remarks.
McArthurs ⁵²	2	0	1	One not benefited.
Eyre ³³	14	10	4	
<i>Chronic.</i>				
French ⁴²	2	2	0	
Ohlmacher ⁹²	2	0	2	
McArthurs ⁵²	11	0	7	Four not benefited.
Illman ⁶⁶	1	1	0	
Eyre ³³	5	2	3	
Loxton ⁵⁰	3	3	0	
Thomas ¹²³	1	1	0	
Lake ⁷⁵	1	0	0	Not benefited.
McDonald ⁵³	6	0	0	Not benefited.
Miller ⁹²	3	3	0	
	<hr/> 51	<hr/> 22	<hr/> 17	12 not benefited.

Vaccines should be tried in this condition, particularly in chronic cases, which, as a general rule, resist all other forms of treatment.

Urethral Stricture.

Ballenger³ has reported 3 cases of urethral stricture, due to the gonococcus, which were benefited by the administration of a vaccine.

Salpingitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Tuttle ¹²⁵	1	1	0	
Fisher ³⁹	2	2	0	
	<hr/> 3	<hr/> 3	<hr/> 0	

The case reported by Tuttle was gonorrhœal salpingitis, while the 2 cases reported by Fisher were the ordinary pyosalpinx.

Septic Endometritis.

Oastler⁹⁶ reports a case of septic endometritis in which *Streptococcus pyogenes* and *Bacillus colon* were isolated from the uterus. The administration of a vaccine made from these organisms resulted in marked improvement in the condition.

Vaginitis (Specific in Children).

Authors.	Cases.	Cured.	Improved.	Remarks.
Ohlmacher ⁹⁹	2	2	0	
Butler ²⁰	12	10	2	
Hamilton ⁵³	67	0	64	One not benefited.
Churchill ²⁷	17	10	7	
Butler ²²	25	0	25	
Ladd and Russ ⁷⁶	3	2	1	
Thomas ¹²⁸	1	0	1	
Hamilton ⁵²	84	76	0	Five not cured: three lost.
	<hr/> 211	<hr/> 100	<hr/> 103	<hr/> 6 not benefited.

In the first series of 12 cases treated by Butler and Long, the average duration of treatment was forty-three days. Ten of the cases were cured and 2 improved. Of 12 other cases studied at the same time, that were receiving routine treatment, only 3 were cured, on an average of fifty-one days for the series of cases. In the cases studied by Hamilton and Cooke, 11 were acute. Of 7 of these cases treated by vaccines, 4 improved rapidly, 2 improved slowly, and 1 was not benefited. They found that in the 4 cases not treated, 2 were benefited and 2 did not improve. They conclude that vaccine treatment has advantages over routine treatment. In 10 cases, both routine and vaccine treatment were used. There was no advantage noted over the cases receiving vaccine treatment alone. They call attention to the fact that while vaccine treatment can be administered in

the home by the physician, routine treatment can only be used in hospitals, and even here there is always danger of mechanical injuries, or even peritonitis, being produced. The prolonged use of the douche in the treatment of cases of this character may also induce the habit of masturbation, and Hamilton and Cooke cite the case of three little girls who were incorrigible masturbators as long as vaginal douches were given, but when the douches were stopped and vaccine treatment begun, the girls ceased the habit. Churchill and Soper had an average of only nineteen days' duration in the treatment of their series of 17 cases. In the second series of 25 cases treated by Butler and Long, the average duration of treatment was forty-three days. Thirteen of these cases were chronic, 11 of which recovered, with an average duration of treatment of thirty-nine days. Hamilton gives the following table showing the results obtained by vaccine treatment compared with irrigation methods:

Treatment.	Cases.	Cured.	Not cured.	Lost.	Per cent. cured.
Irrigation	260	158	53	49	60 per cent.
Vaccine	84	76	5	3	90 per cent.

Average length of time under active treatment by the irrigation method, 10.1 months.

Average length of time under active treatment by the vaccine method, 1.7 months.

DISEASES OF THE SKIN AND ITS APPENDAGES.

Acne.

Authors.	Cases	Cured.	Improved.	Remarks.
Wright ¹⁴³	3	1	2	
Bullock ²⁰	5	5	0	
Ohlmaeher ²²	2	1	1	
Turton ¹³⁴	2	2	0	
Ross ¹¹⁰	2	2	0	
Varney ¹²⁶	9	6	2	One discontinued treatment.
Ross ¹¹¹	5	5	0	
McArthur ⁵²	2	1	1	
Western ¹⁴¹	12	12	0	
Schamberg ¹¹⁵	7	1	3	Three not benefited.
Floyd ⁴¹	2	2	0	
Illman ⁶¹	4	3	0	One not benefited.
Ridlon ¹⁰⁵	1	1	0	
Miller ⁹¹	3	2	1	
Turton ¹³³	8	3	5	
Strubell ¹²⁷	9	4	4	One still under treatment.
Ladd and Russ ⁷⁵	28	6	14	Two not benefited; 6 discontinued treatment.
Wolfsohn ¹⁴⁵	1	1	0	
Fleming ⁴⁰	3	3	0	
White and Eyre ¹⁴²	1	1	0	
Beggs ⁹	2	1	1	
Thomas ¹²³	5	2	3	
McDonald ⁵³	19	7	10	Two not benefited
Fisher ²⁹	4	2	1	One not benefited.
	139	74	48	9 not benefited.

Fleming treated his 3 cases with a mixed vaccine of *Staphylococcus albus* and *Bacillus acne*. This author claims that while the staphylococci are always associated with the pustular lesions of this disease, the acne bacillus is the true etiological factor, and in order to produce an immunity to the disease, vaccines of both organisms must be used.

Carbuncles.

Authors.	Cases.	Cured.	Improved.	Remarks.
Hartwell ¹⁸	1	1	0	
Western ¹⁴¹	2	2	0	
Floyd ⁴¹	1	1	0	
Strubell ¹²⁷	1	1	0	
Wolfsohn ¹⁴⁵	1	1	0	
Turton ¹³³	1	1	0	
Mallanah ⁸³	2	2	0	
Thomas ¹²³	7	6	1	
McDonald ⁸³	3	3	0	
Miller ⁹²	1	1	0	
Fisher ³³	4	4	0	
	<hr/> 24	<hr/> 23	<hr/> 1	

While the number of cases is small, the results achieved with bacterial vaccines in carbuncles is rather remarkable.

Eczema.

Authors.	Cases.	Cured.	Improved.
Schamberg ¹¹⁸	1	0	1
Floyd ⁴¹	1	0	1
Crofton ³³	1	0	1
Miller ⁹¹	1	0	1
McDonald ⁸³	3	3	0
	<hr/> 7	<hr/> 3	<hr/> 4

As to just what role bacteria play in the etiology of eczema dermatologists do not agree. Gilchrist and many other authorities are inclined to think that as the primary factor they are of not much importance. It is agreed, however, that secondary infections are extremely common, and it is probable that it is in these secondary conditions that vaccines may be of use.

Erysipelas.

Authors.	Cases.	Cured.	Improved.	Remarks.
Schröter ¹¹⁶	37	37	0	Two had relapse.
Harris ⁵⁴	1	1	0	
Illman ⁶⁵	2	1	0	One not benefited.
Ross ¹¹²	19	19	0	
McDonald ⁸³	9	8	0	One died.
Thomas ¹²³	2	1	1	
Hoobler ⁶³	1	1	0	
	<hr/> 71	<hr/> 68	<hr/> 1	2 not benefited.

Schorer is of the opinion that the use of vaccines in erysipelas shortens the duration of the disease somewhat. Ross and Johnson compare the results obtained in 19 cases treated with vaccines to the results obtained in 19 cases treated the year previously by internal and external applications. The following table gives the comparison.

	Treated by vaccines.	Routine treatment.
Pyrexia completed in twenty-four hours	7	3
Pyrexia completed in forty-eight hours	7	3
Pyrexia completed after forty-eight hours	5	13
Average duration of pyrexia	3.1 days.	8.9 days.
Complications	1	6
Average duration of illness	12.8 days.	25 days.
Average stay in hospital	11.2 days.	18 days.

Furunculosis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Wright ¹⁴⁷	6	6	0	One case relapsed.
Wright ¹⁴⁸	6	3	2	One not benefited.
Bulloch ²⁰	4	4	0	
Ohlmacher ⁹⁹	3	1	2	
Turton ¹³⁴	3	2	1	
Ross ¹¹⁰	1	1	0	
Thorne ¹³⁰	1	1	0	Three years' duration.
Hartwell ¹⁸	3	3	0	
Varney ¹²³	5	5	0	
Ross ¹¹¹	11	9	2	
McArthurs ⁸²	3	3	0	
Western ¹⁴¹	9	9	0	
Schamberg ¹¹⁵	3	1	2	
Floyd ⁴¹	1	1	0	
Beebe ⁷	3	3	0	
Bristow ¹⁶	1	1	0	
Illman ⁶⁶	1	1	0	
Brittenstool ¹⁷	3	3	0	
Whitmore ¹⁴³	1	1	0	
Strubell ¹²⁶	12	10	1	One not benefited.
Ladd ⁷⁵	7	7	0	
Wolfsohn ¹⁴⁶	5	3	1	One not benefited.
White and Eyre ¹⁴²	1	1	0	
Turton ¹³³	1	0	1	
Hoobler ⁶²	2	2	0	
Mallanah ⁸³	2	2	0	
Rooker ¹⁰⁹	2	2	0	
Beggs ⁹	12	12	0	
Thomas ¹²⁵	6	6	0	
McDonald ⁵³	14	14	0	
Fisher ²³	3	3	0	
Miller ³²	3	3	0	
Strubell ¹²⁷	2	2	0	
	140	125	12	3 not benefited.

That vaccines are of benefit in this condition there can be no doubt, and while there is a very small percentage of cases that for some unknown reason do not react, it is probable that no other method of treatment will accomplish the same satisfactory results. Even with vaccine treatment, however, a very small percentage of the cases relapse.

Impetigo.

Ohlmacher⁹⁹ reports 2 cases of impetigo cured with autogenous vaccines.

Lupus.

Authors.	Cases.	Cured.	Improved.	Remarks.
Ross ¹¹⁰	2	1	1	
Turton ¹³⁴	2	0	2	
Western ¹⁴¹	11	6	4	One not benefited.
Todd and Western ¹³¹	5	1	3	One not benefited.
Richardson ¹⁰³	1	0	1	
Turton ¹³³	3	0	1	Two not benefited.
Carmalt-Jones ²¹	23	3	17	Three not benefited.
	—	—	—	—
	47	11	29	7 not benefited.

Psoriasis.

Two cases of psoriasis treated by bacterial vaccines have been found in the literature; 1 case reported by Ohlmacher was cured, and the other case, reported by Schamberg, Gildersleeve, and Shoemaker,¹¹⁵ was not benefited.

Dandruff.

Fisher³⁹ reports improvement in 2 cases of dandruff treated with a vaccine made from *Staphylococcus albus*.

Sycosis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Wright ¹⁴³	3	3	0	
Bulloch ²⁰	2	1	0	One not benefited.
Turton ¹³⁴	1	1	0	
Varney ¹³³	2	1	0	One discontinued treatment.
Ross ¹¹¹	1	0	1	
Schamberg ¹¹⁶	9	1	6	Two not benefited.
Crofton ³²	1	1	0	
Grant ⁴⁸	1	1	0	
Turton ¹³³	1	0	1	Relapsed.
Strubell ¹²⁸	1	0	1	
Ladd and Russ ⁷⁶	2	0	1	One not benefited.
McDonald ⁸³	4	4	0	
	—	—	—	—
	28	13	10	4 not benefited.

In sycosis, good results are the rule, although sometimes the treatment requires a considerable period of time.

DISEASES OF THE BONES AND JOINTS.

Arthritis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Painter ¹⁰⁰	6	0	0	None of the cases benefited.
Sherman ¹²⁰	5	4	1	
Thomas ¹²³	3	0	0	Not benefited.
	—	—	—	
	14	4	1	9 not benefited.

The treatment of arthritis with bacterial vaccines can never be successful until the true cause of the disease is determined. Painter treated his 6 cases with vaccines made from the streptococcus, the streptococcus and Schuler's bacillus, the streptococcus, staphylococcus, and Schuler's bacillus, and Schuler's bacillus and the pneumococcus. His results were negative in all cases. Sherman's series includes 3 acute, 1 subacute, and 1 chronic case of arthritis. All were treated with a special streptococcic stock vaccine. The chronic case was improved and the remaining cases cured. In the 3 cases reported by Thomas, *Staphylococcus aureus* was the infecting organism in 1 case, *Staphylococcus albus* in 1, and a mixture of the two in the other case. Vaccines made from these organisms were of no benefit.

Gonorrhæal Arthritis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Oehlacher ⁹⁹	2	1	1	Four not benefited.
Cole and Meakins ⁷⁹	15	10	5	
McArthurs ⁸²	1	1	0	
Bristow ¹⁶	1	1	0	
Irons ⁶⁷	31	18	9	
Illman ⁶⁰	2	2	0	
Whitemore ¹⁴³	1	1	0	Three not benefited.
Mainini ⁸⁷	4	0	4	
Ladd and Russ ⁷⁶	11	0	11	
Maute ⁹⁰	4	4	0	
Oastler ⁹⁵	1	1	0	
Dieulafoy ³⁸	18	7	8	
White and Eyre ¹⁴¹	4	4	0	Nine not benefited. Four not benefited.
Eyre and Stewart ³⁸	26	18	8	
Thomas ¹²³	4	2	2	
Hartwell ⁸⁷	51	0	42	
McDonald ⁸³	14	9	1	
Jack ⁷⁰	4	4	0	
Miller ⁹²	1	1	0	
	—	—	—	
	195	84	91	20 not benefited.

In gonorrhœal arthritis the results are usually good, but here also a certain number of cases fail to respond to the treatment. The immunity, however, is of short duration, as would be expected from a study of other gonorrhœal infections, and relapses are apt to occur, especially if a fresh infection of the urethra is contracted.

Rheumatoid Arthritis.

White and Eyre¹⁴² have treated 1 case of rheumatoid arthritis with *Staphylococcus aureus* vaccine and report improvement.

Osteomyelitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Illman and Duncan ⁶⁰	1	0	1	
Hartwell ⁶⁰	4	0	0	Not much benefited.
Wolfsohn ¹⁴⁶	3	0	0	Not benefited.
Thomas ¹²³	2	0	1	One not benefited.
	<hr/> 10	<hr/> 0	<hr/> 2	<hr/> 8 not benefited.

Osteoperiostitis.

Thomas¹²⁸ reports a case of gonorrhœal osteoperiostitis treated with gonococcic vaccine with improvement.

Tuberculosis of Bones and Joints.

Authors.	Cases.	Cured.	Improved.	Remarks.
Turton ¹³⁴	1	0	0	Not benefited.
Painter ¹⁰⁰	7	0	3	Four not benefited.
McArthurs ²³	19	1	15	Three not benefited.
Ogilvy ⁹³	5	0	4	One not benefited.
Illman ⁶⁰	8	2	3	Three not benefited.
Crofton ³³	1	1	0	
Turton ¹³³	5	0	2	Three not benefited.
Smith ¹²⁴	34	11	19	Three not benefited.
Thomas ¹²³	20	0	15	Five not benefited.
	<hr/> 100	<hr/> 15	<hr/> 61	<hr/> 23 not benefited.

This series of cases includes Pott's disease, tuberculosis of the hip-joint and other bones and joints.

DISEASES OF THE NOSE AND THROAT.

Coryza.

Authors.	Cases.	Cured.	Improved.	Remarks.
Harris ⁶⁵	1	1	0	
Benham ¹¹	5	0	5	
	<hr/> 6	<hr/> 1	<hr/> 5	

The case reported by Harris was treated with a vaccine made from *Micrococcus catarrhalis*. Benham treated his case with a mixed vaccine made from *Micrococcus catarrhalis* and *Micrococcus paratetrigenus*.

Hay Fever.

Fisher³⁹ has successfully treated a case of hay fever with a vaccine made from *Staphylococcus albus*.

Influenza.

Fisher³⁹ reports a case of influenza treated with success with an autogenous vaccine made from the influenza bacillus and the pneumococcus.

Atrophic Rhinitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Skillern ¹²²	2	0	2	
Mosher and Kerr ³³	10	0	10	
Fisher ³⁹	1	0	1	
	<hr/> 13	<hr/> 0	<hr/> 13	

The cases of Skillern and Burvill-Holmes were treated with a vaccine made from *Bacillus mucosæ*. The 10 cases of Mosher and Kerr were treated with a mixed vaccine of *Staphylococcus aureus*, *albus*, and *citreus*. These authors state that improvement was noted in all cases, and particularly in the bad ones. The headache, the odor, the large crusts, the dryness of the throat, were improved in all cases, and in many of them cured. Fisher's case was treated by a vaccine made from *Staphylococcus citreus*.

Tuberculous Laryngitis.

Illman and Duncan⁶⁶ report a case of tuberculosis of the larynx treated with tuberculin with improvement. Two cases treated by Carmalt-Jones²³ were not benefited.

Sinusitis.

Beck⁸ treated 3 cases of sinusitis, 1 an acute unilateral, 1 a sub-acute unilateral, and 1 a chronic polysinusitis with staphylococcic vaccine. All 3 cases were improved.

DISEASES OF THE EYE AND EAR.

Gonorrhæal Conjunctivitis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Ohlmacher ⁹³	3	2	1	
Eyre and Stewart ³³ . . .	1	0	0	Not benefited.
Miller ⁹²	2	2	0	
	<hr/> 6	<hr/> 4	<hr/> 1	1 not benefited.

Corneal Ulcer.

Allen¹ reports 2 cases of corneal ulcer from which the pneumococcus was isolated in 1 case and a small unknown micrococcus in the second. Vaccines were made from the respective organisms and cures occurred in both cases.

Hypopyon.

Allen¹ treated 3 cases of hypopyon with autogenous pneumococcic vaccines. Two of the cases were cured and the other improved.

*Iritis.**Gonorrhæal.*

Authors.	Cases.	Cured.	Improved.	Remarks.
Eyre and Stewart ³⁵	4	3	1	
Miller ⁹²	1	1	0	
Shumway ¹²¹	1	1	0	

Tuberculous.

Ross ¹¹⁰	1	0	1	
Ross ¹¹¹	1	0	1	
	<hr/> 8	<hr/> 5	<hr/> 3	

Phlyctenular Infections.

Gradle⁴⁷ reports 9 cases of phlyctenular infections due to staphylococci. Staphylococcic vaccines gave satisfactory results in the treatment of all 9 cases.

Mastoiditis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Conners ³⁰	3	0	2	One not benefited.
Hoobler ⁵²	1	1	0	
Scott ¹¹⁸	1	1	0	
	<hr/> 5	<hr/> 2	<hr/> 2	1 not benefited.

Otitis Media.

Authors.	Cases.	Cured.	Improved.	Remarks.
Beek ⁸	4	0	4	
Todd and Western ¹³¹	3	1	2	
Trimble ¹³²	4	4	0	
Conners ³⁰	7	2	3	Two not benefited.
Hoobler ⁵²	2	2	0	
Mallanah ⁸⁸	1	1	0	
McWaters ⁴⁵	1	1	0	
Thomas ¹²⁵	1	0	0	Not benefited.
Jacobs ⁷¹	6	2	4	
Christie ²⁶¹	6	6	0	
McDonald ⁵³	3	2	0	One not benefited.
	<hr/> 38	<hr/> 21	<hr/> 13	4 not benefited.

The 3 cases reported by Todd and Western were mixed tuberculous and staphylococcic infections. The case reported by Mallanah was due to *Bacillus pyocyaneus*. The remaining cases were mixed coccic infections. Conners is not sure that vaccines possess any particular merit over the routine treatment of this condition, and thinks that, while cures occur, prolonged treatment is usually required. He believes, however, they are of value in very obstinate cases, and should be tried when other means fail.

MISCELLANEOUS INFECTIONS.

Local Sepsis.

Authors.	Cases.	Cured.	Improved.	Remarks.
Oblmacher ⁹³	2	2	0	
Rodd ¹⁰⁸	1	0	1	
Hartwell ⁵³	1	1	0	
Gildersleeve ⁴⁴	1	1	0	
Beebe ⁷	2	1	1	
Ballenger ³	1	0	1	
Floyd ⁴¹	3	2	1	
Richardson ¹⁰³	1	0	0	Not benefited.
Brock ¹³	1	1	0	
White and Eyre ¹⁴²	5	5	0	
Wolfsohn ¹⁴³	3	1	0	Two not benefited.
Hartwell ⁶⁰	41	0	41	
Hoobler ⁶³	2	2	0	
Thomas ¹²³	18	6	4	Eight not benefited.
McDonald ⁶³	7	2	3	Two not benefited.
Fisher ³⁹	17	10	2	Five not benefited.
Strubell ¹²⁷	2	0	0	Not benefited.
Sherman ¹²⁰	1	1	0	
Turton ¹³³	2	1	1	
Illman ⁶⁰	1	1	0	
Beggs ⁹	1	1	0	
Evans ³⁷	1	1	0	

Tuberculous Infections.

Carmalt-Jones ²³	50	10	29	Eleven not benefited.
Wolfsohn ¹⁴³	1	0	1	—
	165	49	85	31 not benefited.

The above series of cases includes such conditions as cellulitis local abscesses, fistulas, sinuses, and other conditions of local infection.

Postoperative Infections.

Authors.	Cases.	Cured.	Improved.	Remarks.
Sebottmuller ¹¹⁷	1	1	0	
Weinstein ¹⁴⁰	4	2	1	One not benefited.
Turton ¹³¹	2	0	2	
Thomas ¹²³	9	2	4	Three not benefited.
Hartwell ⁶⁹	1	1	0	
Hartwell ⁶⁰	22	22	0	
	39	28	7	4 not benefited.

Tuberculous Meningitis.

Turton and Parkin¹³⁴ report a case of tuberculous meningitis treated with tuberculin without success.

Diabetes Mellitus.

King⁷³ isolated *Saccharomyces cerevisiæ* from the blood of 16 diabetic patients. Six of these patients were treated with a vaccine

made from the fungus, with general improvement in their condition. The reduction in the amount of sugar in the urine was not marked, but the acetone and diacetic acid disappeared. King had the patients still under treatment at the time of writing.

Miller⁹² reports 4 cases of furunculosis with glycosuria. When the staphylococcic infection was treated with vaccines the glycosuria cleared up.

Lack of Nutrition in Mania.

Bruce¹⁹ has noted that the most common bodily disorder in patients suffering with chronic mania is lack of nutrition. He treated 11 such cases with a polyvalent vaccine made from seven strains of streptococci obtained from the blood, urine, and feces of the patients. Four of the patients recovered from the mania, but what was more surprising, was the improvement of nutrition in 8 of the patients receiving the vaccine. One patient gained twenty-eight pounds in six months, another twenty-six pounds in five months, and there was marked improvement in the nutrition of 6 of the other patients receiving the vaccine.

Not including the prophylactic inoculations, the total number of cases treated by vaccine therapy collected in this series is 2332. Of these, 2000, or 86 per cent., were cured or improved; 251, or 10 per cent., were not benefited; and the remaining 79 cases discontinued treatment, or were lost. Three hundred and six of the cases were general infections, and of these, 274, or 88 per cent., were cured or improved, and 28, or about 9 per cent., not benefited. The series includes sixty-seven different conditions. These figures signify little except in pointing out the tremendous, almost unlimited, field that vaccine therapy may cover. In no instance was serious harm caused by the use of vaccines, although Leary⁷⁷ reports 2 cases that, through an error, had received 10,000,000,000 of dead staphylococci at a single dose. One of these cases experienced no ill effects whatever; the second case, however, collapsed a few hours after inoculation, but responded to strychnine and the application of hot water bags, and had practically recovered in fifteen minutes.

It is believed that there are certain factors that might have modified the above results even more favorably had they been followed. Among these may be mentioned:

Uniformity of Doses. It is realized that in order to arrive at just what is the proper dose of dead bacteria to employ in a given condition, it is necessary to study the effect of various sized doses. It is also true that the number of bacteria inoculated at one time depends upon the nature of the disease, whether it is acute or chronic, on the interval between doses, and on the condition of the individual. However, in reviewing the literature, it is often found that one observer treats furunculosis with 10,000,000 dead staphylococci at a dose, while another gives doses of 1,000,000,000; or one author

gives 5,000,000 dead gonococci and another 500,000,000 in an identical condition. The question arises, whether the too large doses may not do harm or the too small ones be of no benefit; at least, it would seem that under the same circumstances, better results might have been obtained had more uniform doses been employed. I have in preparation an analysis of the various doses employed by different observers, and the results achieved, in the hopes of arriving at something near a standard dose of the various organisms.

Intervals between Doses. About the same applies to the intervals between doses as has been described for the size of the doses, both as regards the disease and the condition of the patient. Some authors advise daily injections, while others allow intervals of two weeks, or even a month, between inoculations. Here, too, better results might have been obtained if more uniformity had been followed. Of course, in much of the work done the opsonic index has been used as a guide, but this is subject to such wide variations, that it has only served to complicate matters, and it is now generally believed that the opsonic index is of little value except in the hands of experts.

Stock Vaccines. While stock vaccines are undoubtedly useful in certain conditions, their injudicious use in the hands of careless physicians and unskilled diagnosticians has probably done more to discredit bacterial therapy than any other one thing. The practice of injecting various kinds of dead bacteria or mixtures of vaccines in conditions of obscure etiology in the hope that one or the other may do good, is to be severely condemned.

Preparation of Vaccines. The proper preparation and standardization of a vaccine requires no little skill, and should not be entrusted, as is often done, to internes. Slight errors in standardization are unavoidable, even when carried out by practiced hands, and these errors may assume undesirable proportions in unskilled hands. The methods of killing bacteria are also at variance. Some authorities advise high temperature for short intervals, others low temperatures for long intervals, others low temperatures for short intervals and the addition of antiseptics; and still others, the use of antiseptics alone.

In conclusion, it is suggested that vaccines should only be employed, first, in general infections after blood cultures have been made and the infecting organism identified by an experienced bacteriologist; second, in local infections, in which the organism has been isolated and identified, or in which the symptoms are so marked that a mistake in diagnosis is beyond a possibility.

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MALIGNANT DISEASE AS A PROBLEM OF MODERN SURGERY.¹

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THERE seems to be no question among qualified observers that malignant disease in all its forms is gradually becoming more prevalent among the civilized races. Rodman, Billings, and others have collected statistics showing this to be the case in the United States, and the same fact seems to be established as regards Germany, England, and other countries. And more than ever the surgeon is called upon to deal with this scourge of humanity. The time has passed when those whose duty it was to assuage the sufferings of mankind can be idle and allow any form of disease permanently to baffle them. It is but a short time since all but the most superficial and slight forms of malignant disease were regarded as inevitably fatal and, indeed, were hardly given the benefit of any attempt at treatment, unless perhaps we may consider as treatment the relief of pain only.

In all forms of malignant disease we face a pathological process the true significance of which has so far remained beyond our understanding. Bacteriology and pathology, hand in hand, have shown us the cause and nature of pus infections; they have made clear the origin and fundamental process of many of the infectious diseases. Syphilis, whose causative factor was found but five years ago, bids fair soon to be under control. At the same time, preventive medicine has under favorable conditions minimized such diseases as typhoid fever, cholera, and yellow fever. In comparison

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with the great strides which we may observe on every hand in other fields of medical research, we still are well nigh powerless when it comes to malignant tumors.

Let it not be supposed that our efforts have been fruitless. No one who has followed the trend of surgery or of cancer research can fail to be convinced that our investigators are upon the right track and that we must soon emerge from the darkness of comparative ignorance into the light of definite knowledge.

Malignant disease has been known for centuries; it is, as I have said, upon the increase. There is not a community in which it is not present, and every day in one form or another it has its victims. Countless men have labored to discover the cause of this mysterious process, and are still doing so, yet we do not know the etiology of malignant growths.

The theory that perhaps carcinomas and allied growths are due to the development of misplaced embryonal tissues in localities where their growth has made them pathological has been definitely set aside. The transplantations of neoplasms, the apparent infectiousness of certain forms of cancer in fish, and many other pathological facts concerning the dissemination and minute structure of carcinoma renders this view of their origin untenable.

With the rise of bacteriology there came the hope that within the field of simple or even unicellular vegetable organisms we might find the causative factor of malignant processes. A few years ago this, perhaps, was our only hope. It also has failed us. Certain oversanguine investigators have from time to time declared this or that bacterium to be the essential factor in carcinoma. Doyen still asserts that his *Micrococcus neoformans* "is the specific agent at fault." I am convinced that there is no form of germ life which has as yet in any way been proved to be responsible for any form of malignant growth.

In later years again protozoan diseases came to the forefront. With the spread of civilization and commerce into tropical and semitropical countries it was found that disease about the equatorial regions was largely caused by these forms of animal life, such as trypanosomes. Sleeping sickness, kala-azar, and other diseases were found to be forms of trypanosomiasis. The brilliant investigations of Bruce, Leishmann, Koch, Laveran, and others have placed the study of animal protozoan life on a par with bacteriology. Even before the investigations into the protozoa which affect the human species we were able to discover that the lower animals, rodents, fish, and birds, have many diseases caused by trypanosomes. But there has never been any evidence adduced to encourage the hope that in the domain of protozoa—either trypanosomes or hematocytes—we have the solution of the cancer problem.

There have been certain recent investigations into the carcinomas and sarcomas of the lower animals, particularly of mice,

which have thrown much light upon our conception of both the transmissibility of malignant growths and upon the production of a certain degree of immunity toward malignant processes. They have demonstrated that certain mouse tumors, while not infectious for other species of animal life, can be transplanted almost indefinitely from host to host in the same species. And not only this, but that they generally correctly transmit the characteristics of the original tumor. Moreover, after repeated transference of tumors they seem to lose their virulence, so that spontaneous cure may result, and in such mice there is established an immunity to subsequent inoculations. There has been but one instance in the human being of the use of body fluid from a patient who had apparently had a spontaneous cure of carcinoma. This is the well-known instance reported by the late Dr. Hodenpyl. Perhaps such serum treatment may offer us something of value in the future.

Before leaving the subject of etiology and pathological physiology of malignant growths I wish to call attention to several points. Recent studies upon the thyroid carcinoma of fish have seemed to establish the fact that certain forms of malignant growths in the lower animals may assume more or less epidemic characters. It is true that it has been asserted that the specific tumor mentioned is not a true carcinoma, yet it resembles it sufficiently to be so classed. While it is true that carcinoma is more prevalent in human beings in certain localities and times, nothing has ever shown us that it is directly transmissible in the way that infectious diseases are.

The influence of diet and especially of water in causing malignant growth is as yet not determined; there is some evidence, however, that the specific cause of thyroid carcinoma of trout is always present in certain bodies of water. An interesting fact in this connection mentioned by Gaylord is that puppies brought to such a body of water known to be infected almost without exception develop thyroid enlargement.

The nearest approach to transmission of carcinoma or other malignant growth in the human species we find in the occurrence of chorion epithelioma. This is practically a malignant growth originating by the transplantation of remaining foetal tissues into the maternal organism, and offers other interesting peculiarities, of which I shall speak later. The following is an example:

Mrs. X., aged twenty-four years, has given birth to one child. Three months after the birth of the child the patient commenced having metrorrhagia, which increased in severity, but without pain. At the time of the operation, curettage was accompanied by such severe hemorrhage that it was deemed best to do vaginal hysterectomy. Pathological examination of the uterus showed chorion epithelioma. The patient is now, four years after operation, entirely well.

Barling has recently reported an instance of spontaneous recovery from chorion epithelioma, ordinarily so virulent.

Heredity was formerly supposed to play an important part in the causation of malignant neoplasms. While I believe that it is undoubtedly true that a patient may have inherited from his ancestors a form of body tissue so vulnerable to malignant invasion that he may be considered predisposed to it, yet I have never seen an undoubted case of inheritance of malignant growth.

Trauma has always been known to play an important part in at least giving rise to a favorable situation for the growth of carcinoma, if not actually causing it. The classical examples of the preponderance of lip epitheliomas in smokers and the infrequency of carcinoma of the cervix uteri in those women who have never borne children (5 per cent. only, Bland-Sutton), are so well known that they need but be mentioned. Abdominal surgery has shown the influence of other than mechanical trauma. Thus, we know that not infrequently carcinoma is implanted upon pyloric ulcer. Mayo has found this change in 54 per cent. of cases, while Moynihan and Fenwick have also called attention to the same feature. There can be no doubt, then, that previous traumatism is in part responsible for the occurrence of malignant tumors.

The most interesting form of malignant growth caused by trauma, other than that of the purely mechanical variety, is the skin carcinoma caused by continued exposure to the x -rays. The exact mode or action of the x -rays in giving rise to malignant degeneration in skin irritated by the too frequent exposure to the rays has not yet been determined.

Histological studies upon mouse cancer and others have given us an insight into the possible spontaneous cure of carcinoma. They have shown that the growth of a cancer is not, as was formerly supposed, a steadily progressive and irresistible process. In every implanted carcinoma or mixed tumor there is a constant endeavor of the healthy body cells to overcome the newcomer by "fibrous strangulation," as it may be called. The newgrowth, while it becomes vascularized by the promotion of a connective tissue stroma which the host supplies, is, nevertheless, continually attacked. The host attempts to surround and gradually crush the malignant growth. At times the process appears to be entirely successful. The complete encapsulation of malignant emboli within blood-vessels and in the lungs is another evidence that the host is not always losing, but is overcome, so to speak, by successive changes of the malignant growth.

Instances of spontaneous recovery from carcinoma and other malignant growths are not unknown in human beings. The recovery of patients suffering from pyloric growths after exploratory operation occurs at times. Involution of scirrhus of the breast has been observed on numerous occasions.

But perhaps the most encouraging feature of all our experimental and chemical evidence is the undoubted fact that all malignant growths are shown to be purely local processes in their onset. Examination of early carcinomas and sarcomas in human beings—some accidentally discovered after removal of a part at operation—prove that they begin as well-localized foci. The same is true of experimentally produced carcinomas. How important this must be is very evident. If we could happily arrive at a diagnosis before the lesion has spread beyond its limited confines the problem of treatment would take on an entirely different aspect. Surgical interference in the early stages of all but a few inaccessible malignant growths would doubtless cure them all.

In addition, before considering the practical side of the question at issue, I would call attention to the difference in malignancy of growths pathologically similar in corresponding areas in different patients. Spontaneous cure we know is possible. Occasionally we find groups of tumors the microscopic characteristics of which show them to be true carcinomas, yet their clinical course is markedly benign. Carcinoma of the appendix vermiformis belongs to this group. Its location surely would predispose to lymphatic distribution, yet it is almost unknown for one to spread or give rise to metastases.

Granted, then, that carcinoma is at its beginning essentially a localized process, it is evident that early recognition and prompt removal are indicated in every case if possible.

The diagnosis of malignant disease has made considerable strides, yet we are still compelled to rely practically entirely upon clinical findings. The laboratory perhaps enables us to discover earlier evidences of mild anemia than we may appreciate by examination, but there its usefulness ends. Nevertheless, certain cases of carcinoma and sarcoma, even when widely invading important internal structures, do not cause anemia. I have lately operated upon a pyloric carcinoma involving the surrounding tissues to a great extent, in which the hemoglobin was 95 per cent., the red blood cells, 5,000,000. The highest red blood count I have ever observed was in a case of sarcoma of the retroperitoneal glands. There has not yet been discovered any specific serum or hemolytic reaction in patients suffering from cancer. A number have been suggested, but are equal in their lack of true value. The chemistry of the blood, however, is an ever-advancing science, and it is conceivable that some such reaction may in the future be discovered. Since there are so many different varieties of malignant tumors, it seems hardly likely that one reaction would suffice for all of them, even carcinoma, and still less for sarcoma. So far the serum reaction for carcinoma have proved but a false hope, defective and not valuable.

Malignant growths as to diagnosis divide themselves into several

classes. We have always been more easily able to ascertain the true nature of superficial growths, for they are visible and palpable. Two factors, however, enter into consideration here. The first is the varying malignancy of epithelial tumors in different subjects, and the second is the frequent early glandular metastasis in cases which locally show but a slight tendency to spread.

It is in the diagnosis of malignancy within the cavities of the body that we have made most progress, and I can say with assurance that this has been due to the surgeon more than the clinician or pathologist. I have often spoken of "autopsy in vivo," of the investigation of pathological processes which the surgeon can observe during life, whereas they are hidden to the internist. To illustrate my point I need only mention a few concrete examples.

Carcinoma of the stomach was formerly diagnosticated only by three points—cachexia, palpable tumor, and pyloric obstruction. I maintain that none of these are diagnostic symptoms of stomach cancer; they are symptoms of a failure to recognize it early and a reflection upon anyone who waits for their appearance before diagnostivating the condition. Our carefully taken histories of the present day combined with prompt surgical intervention enables us to achieve results which would formerly have been considered impossible.

By careful and persistent comparison of case records with operative findings and postoperative histories, we have come to recognize what might be called the symptom complex of incipient gastric carcinoma.

Occasionally there comes to the hands of the surgeon a case of carcinoma of the stomach in its earliest stages, yet in the vast majority of instances the sufferer from malignant disease has been treated for months for anacidity, dyspepsia, or nervous dyspepsia. The anemia has progressed unnoticed until it is evident that it attracts the patient's own attention. Progressive emaciation has been attributed to lack of nourishment and faulty metabolism. And all the while there has been a picture of progressive tissue change such as only malignant growth could cause.

I am firmly convinced that every case of persistent dyspepsia in persons beyond middle age should at once be studied with reference to the possibility of cancer. Here again our laboratory tests fail us. Examination of the stomach contents in early cases of carcinoma means nothing. Late, indeed, when retention occurs, it shows that the stomach contents are undergoing putrefaction. The Oppler-Boas bacillus, once considered as diagnostic of carcinoma of the stomach, signifies nothing other than the stagnation of the food within the stomach and its fermentative destruction.

The signs of early carcinoma of the stomach, which as we know is generally pyloric or prepyloric in location, are not always clear: far from it. The signs of early upper abdominal disease, whether

of gastric, biliary, or pancreatic origin, are in many ways similar; yet in a patient beyond middle age in whom anorexia and particularly an aversion to meat suddenly begins without apparent cause and, insidiously progresses, in whom there is a vague gastric distress, a beginning anemia, and a steady if slight loss in weight, we must always suspect malignant disease. And if the condition does not show marked response to the ordinary hygienic and dietetic measures, the surgeon should be called upon to discover and remedy the fundamental cause of the symptoms.

No one could be more opposed than I to the exploratory operation when this is taken to mean the opening of the abdominal cavity to cover the shortcomings in knowledge of the surgeon. No one is less prone to perform such an operation when it seeks to do away with competent and continued study of a case. Yet there are, and always must be, instances, especially within the range of abdominal conditions, in which we offer the patient a far better chance of recovery by early and perhaps *useless* operation than by delay and *surely* useless operation.

With all our progress in the early diagnosis and earlier treatment of gastric carcinoma, our ultimate results are still most discouraging. How few of our cases come to us early enough to *cure*. How few cases remain well after even our most radical measures. Bloodgood has well said that in malignant disease the clinical diagnosis is difficult in inverse ratio to the duration of the disease. This is particularly true in gastric lesions. We must then of necessity operate in some cases in which our diagnosis is not confirmed if we are to seize upon the favorable moment for any of those in which we have correctly appreciated the lesion present.

In speaking of trauma as a factor in the causation of malignant disease I have mentioned the frequency with which ulcer gives rise to carcinomatous degeneration. Wright has lately emphasized this point. We may almost speak of gastric ulcer when it is chronic and associated with much induration as one of the so-called pre-cancerous states.

The duty of surgery in the prophylactic treatment of cancer should not be lost sight of. Since the role of ulcer in the causation of gastric carcinoma has been clearly demonstrated, who can deny the need of prompt and proper surgical treatment of gastric ulcer? Who can tell how many cases of this disease which have shown temporary improvement under medical treatment have in after years progressed to carcinomatous degeneration at the site of the ulcer? There is in all probability even some chance of the degeneration of a temporarily healed ulcer. There can be no question about the superiority of surgical treatment in its immediate results, and particularly in its prevention of future severe complications.

Carcinoma of the gall-bladder and biliary passages is fortunately

rare, though it is seen occasionally in the course of any extended series of operations upon the biliary tract. In practically every instance it is secondary to the presence of gallstones. In fact, carcinoma of the gall-bladder presents, perhaps, our best example of malignant growth in an internal viscus as a sequel to purely mechanical trauma. Here again the surgeon is often helpless when the condition has been well established, yet is able to remove and cure the possible future cause of carcinoma. The surgical treatment of gallstone disease is cancer prophylaxis in its most evident type.

Along the alimentary tract from the stomach to the rectum carcinoma is not at all infrequent. Here again we often see examples of cases treated palliatively for long periods of time until the very positiveness of the diagnosis proclaims at the same time the hopelessness of treatment. In intestinal carcinomas we have not the age of the patient as so sure an index of the probable nature of the disease as in gastric carcinoma. Carcinomas and especially sarcomas of the large and small intestines are by no means unknown in even young adults. By far more frequent are growths of the large intestine, and fortunately for us they are easiest to diagnosticate. When we see a patient, particularly at the cancer age of life, who presents evidences of intestinal indigestion, with perhaps alternate constipation and diarrhœa and the occasional presence of blood in the stools, we should at once think of malignant change, even in the absence of a palpable tumor or marked cachexia. In this connection we have a laboratory test which is of considerable value. The test for occult blood enables us often to detect the presence of minute quantities of blood in the feces which otherwise it would not be possible for us to observe. Here again I would urge the value of an exploratory operation in the true sense of the word, for we do not have long-continued and marked disturbances of intestinal function without marked pathological causes therefor.

Perhaps even more than is the case with disease of the stomach, physicians, as a rule, are prone to disregard the value of a careful anamnesis and physical examination of the patient in intestinal disorders of the chronic variety. Many patients, indeed, with rectal growths go from one physician to another before one makes a complete examination, digital and instrumental.

Intestinal growths in their early stages present one of the most favorable types for operation, and their location generally permits of complete removal with a large area of healthy adjacent tissue and the corresponding glandular lymphatic area. Even in the comparatively late stages of the disease, unless the lymphatic distribution has become too greatly infected or the growth has spread too far into the mesentery or surrounding viscera, our permanent after-results are often suprisingly good. The later studies upon the relationship of various segments of the intestinal canal with

abdominal lymphatic chains enables us often to remove the whole affected lymphatic area and those glands within it not yet involved. Moreover, the improvement in technique brought about by the use of various methods of mobilization of the large gut by swinging it partially free of its mesenteric and peritoneal attachments while preserving the blood supply has enabled us to overcome many of the mechanical difficulties formerly associated with resection of the bowel.

Carcinoma of the bladder has, as a rule, been regarded as hopeless. The cystoscope has proved of vast value in this field. By its use in the hands of skilled men we are able to diagnosticate malignant growths within the bladder at a stage when formerly they could not be correctly diagnosticated. There can be no excuse for allowing a case of simple hematuria, terminal hematuria, or persistent hematuria to progress without having the source of the abnormal urinary constituents localized by the aid of the cystoscope and the ureteral catheter. An even later stage of procedure within the bladder is the removal of small portions of tumors for diagnostic purposes by the operating cystoscope. This is a method of treatment still in its infancy. Cases have even been reported of the removal of benign myomas by electrothermic instruments within the bladder guided by cystoscopic observation. I cannot but feel that the proper way to approach bladder growths is by the open method through the abdominal incision.

Formerly, practically all bladder operations were performed extraperitoneally, and by this method there is no doubt that we have often failed to secure proper exposure of the field and complete removal of the growth. The newer method of intraperitoneal approach to the bladder probably offers us the solution of the complete extirpation of growths which have deeply invaded the fundus of the viscus. And in view of the success which has attended such procedures we should not hesitate to apply them when they are indicated. There is no doubt that the intraperitoneal bladder operation has passed beyond the experimental stage and is upon a firm footing.

The field of gynecological surgery offers one permanent example of the need of educating the laity to an appreciation of the insidious way in which cancerous growths have their onset. It has been a matter of great difficulty to educate the medical profession in the knowledge that every metrorrhagia in a woman at or near the menopause is a sign which must be most carefully watched. Often, indeed, such cases progress to a complete cessation of the uterine flow without further difficulties than those dependent upon the resultant anemia. Some, however, indicate by their progress that there is some uterine condition other than a mere myopathic or vascular one. Among the laity, indeed, such matters have been treated as trifles until uterine carcinoma at an inoperable stage

makes itself manifest. The importance of at once consulting a physician upon the appearance of a fetid leucorrhœa, or one which presents even the smallest portion of blood, cannot be too strongly insisted upon.

Of late years there has been a systematic effort in Germany to reach the laity and instruct them as regards this matter. The effort is a laudable one. But we must not lose sight of the fact that many of our own profession have not yet come to realize the importance of the early recognition of uterine carcinoma of all varieties and the hopelessness of late operations in this condition.

The operation devised by Wertheim and used in various modifications by American operators has for its object the extirpation of a carcinomatous uterus, together with adjacent tissues, and particularly the pelvic lymphatics about the great vessels into which its infection is liable to spread. No one can deny that every attempt at radical operation in carcinoma is better than a palliative one if it does not involve too high an initial mortality. Yet I am certain that operations at a stage of uterine carcinoma when such an extensive procedure is necessary must be in the vast majority of cases futile. Such has been my experience and that of many others.

Our hope in cancer of the uterus lies in two directions: (1) In the education of physicians to recognize its early manifestations, and the education of the laity as regards prompt professional advice in seemingly minor pelvic conditions; and (2) in the use of the microscopic and pathological diagnosis in every case of curettage for intra-uterine disease not directly within the cancer age. I would mention also the recognition of the fact that erosions of the uterine cervix beyond middle age are far more often malignant than has been supposed, and in their earliest stages are favorable cases for radical and completely curative operation. But by far the widest field for the use of the immediate pathological diagnosis in determining the scope of operation and its prognosis we find in malignant tumors of the breast. It is a well-known fact that every tumor of the breast beginning at the so-called cancer age is sufficient to cause the physician the gravest apprehension and should be treated as if it were a malignant growth if a clinical diagnosis alone is to be depended on. This also holds true of all breast tumors of long standing which suddenly show a marked acceleration of growth.

Recent pathological studies have shown us that the borderline between benign and malignant tumors of the breast is by no means a definite one, and that tumors in their incipiency benign may later undergo rapid malignant change. Moreover, we have ample statistical evidence of the frequent occurrence of malignant tumors of the breast in early adult life and even in adolescence.

By careful training of our faculties of observation and long experience, we can, no doubt, attain a degree of certainty in the

macroscopic diagnosis of breast tumors which closely approach that of a rapid microscopic examination. Yet our success with frozen sections has been such as to establish them firmly as an important aid. In breast tumors especially, a frozen section will, on the one hand, often demonstrate to us the uselessness of a radical operation in a growth previously supposed to be malignant, and, on the other hand, will often show an apparently simple chronic mastitis or fibro-adenoma to be a growth which is beginning to show the characteristics of malignant change.

In my own clinic frozen section diagnoses have been almost without exception correct. This has also been the experience at the Massachusetts General Hospital, at the Johns Hopkins Hospital, in the clinics of the Mayo brothers at Rochester, Minn., and in many other institutions.

When we have established the malignancy of a breast tumor by clinical diagnosis or frozen section it is imperative to perform a radical operation. The recent investigations of Handley upon the spread of malignant growths of the breast by the invasion and spread in successive tissue layers and the method of spread by means of the lymphatics make it necessary to remove both the subjacent tissues and the axillary glandular structures.

It has sometimes been questioned whether a radical operation when the axilla is not invaded will not spread rather than avoid infection, but this may safely be answered in the negative.

An interesting fact pointed out by Bloodgood is that, of the recurrences in breast tumors observed by him in a series of cases from Halsted's clinic, many were in cases supposed to be favorable and consisted of carcinomas within the skin scar. He attributes this to the disinclination of the surgeon to perform most radical operations when a less complete one would seem sufficient. I must agree that no matter how favorable the growth, if we are to perform a radical operation, it should be complete in order to give us the best chance of permanent cure, even when a less mutilating procedure might seem sufficient.

It will be seen from the foregoing remarks that the problem of treatment and cure of malignant disease depends entirely upon early diagnosis and surgical treatment. Perhaps the only instance in which of late years it has seemed that our procedures have been too radical has been the case of sarcomas of bones. Bloodgood has lately pointed out that many of these, especially sarcoma of bones in the extremities, which was formerly treated by the most radical procedures, has seemed to recover with simply local palliative operation. It is, indeed, true that perhaps we have been too radical, yet the danger that we may become too conservative in dealing with malignant neoplasms of bones must not be lost sight of.

There is every reason to hope that at some time in the future

there will be discovered not only the specific cause of malignant growths, but also some way of recognizing them earlier than we are at present able to do by clinical methods; and I am convinced that in the course of time experimental research will show us not only the cause of malignant tumors, but will point the way to some other method of cure than by surgical intervention. But until this time arrives, and until we are convinced that our non-operative methods are absolutely certain to cure, we must rely entirely upon early and radical surgery.

As I have stated before, all carcinomas are in the early stages purely local and, unless in some entirely inaccessible place, curable. For the present we must exert all our energy toward refinement of diagnosis and perfection of technique; in this way only will our late results in the treatment of malignant growths show improvement.

THE THENAR AND HYPOTHENAR TYPES OF NEURAL ATROPHY OF THE HAND.

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THE types of neural atrophy of the hand, to which I shall direct attention are unaccompanied by sensory disturbances, and for this reason are of especial clinical interest from their rather close resemblance to the early stage of the progressive muscular atrophy, of the Aran-Duchenne type. I believe that many of these cases are either interpreted as such or are regarded as very doubtful. The frequent association of the two affections (neural and medullary) with occupations requiring overuse of the hands and arms enhances the similarity.

It may be said, in general, that the localization of occupation neuritis in the upper extremity is by no means infrequent, and is recognized by all systematic writers on this subject. There are, however, associated sensory symptoms in the distribution of the affected nerve, which constitute an important part of the symptom complex. In literature these cases are usually designated by the name of the occupation which was instrumental in the production of the lesion: a rather crude manner of classifying such affections of the nerve trunks, as a variety of different occupations may produce the same lesion at the same level of the nerve trunk, providing the character of the movement required is the same.

In other words, it is not so much the nature of the occupation as the character of the movements and its frequent repetition, which plays the chief role in the etiology of the professional palsies.

The exposed and superficial situation of some nerve trunks and their relation to bony prominences and tendons are also important factors.

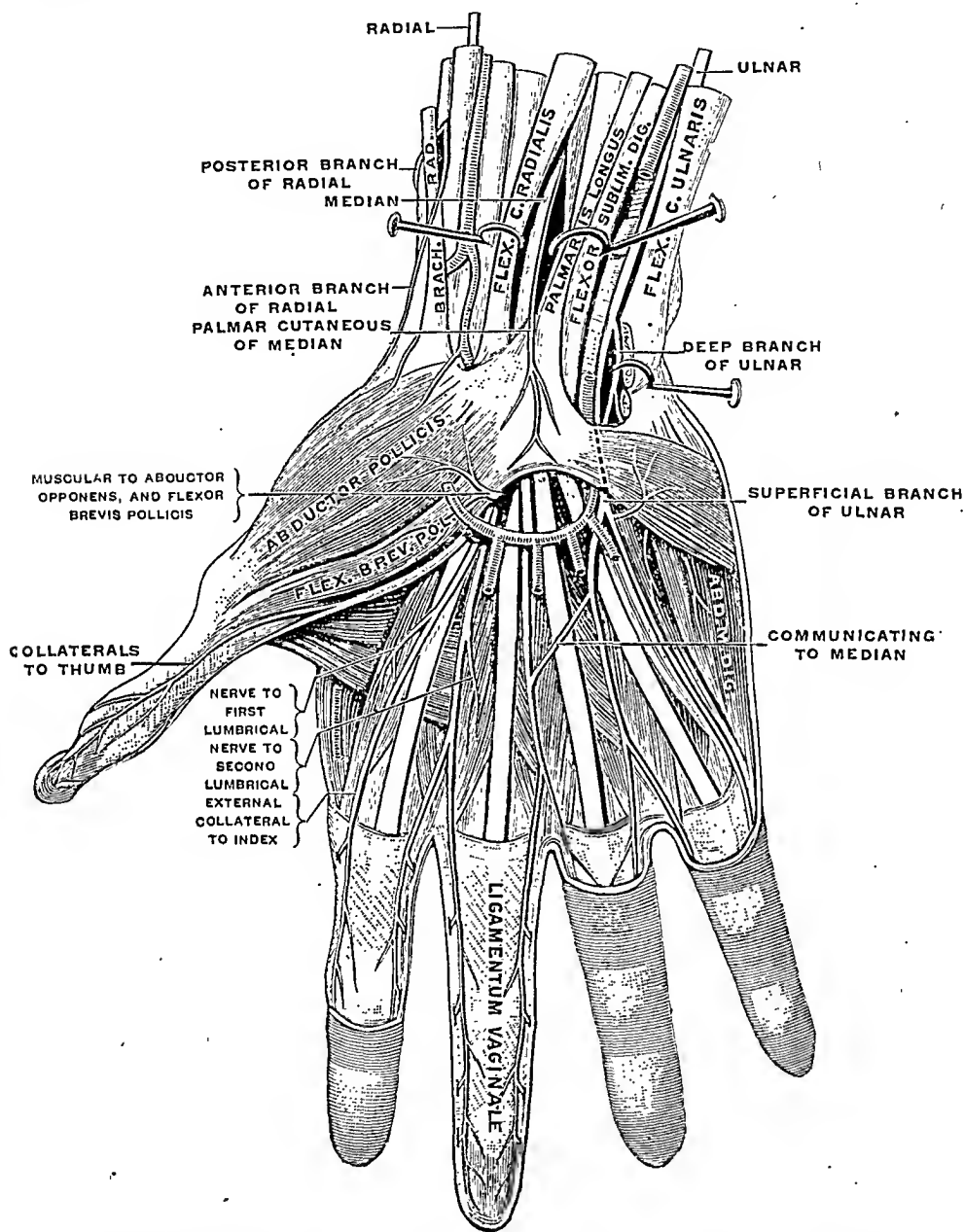


FIG. 1 (Testut's Anatomy).—Showing the superficial and deep palmar branches of the ulnar nerve, and the branches of the median nerve in the hand before removal of the anterior annular ligament.

The general constitutional condition, as well as intoxications of various kinds, also deserve consideration as predisposing factors. It is not uncommonly observed that a certain occupation may have been pursued for many years without ill effects, when a reduction

of the general health, or alcoholic excess, is rapidly followed by the symptoms of neuritis.

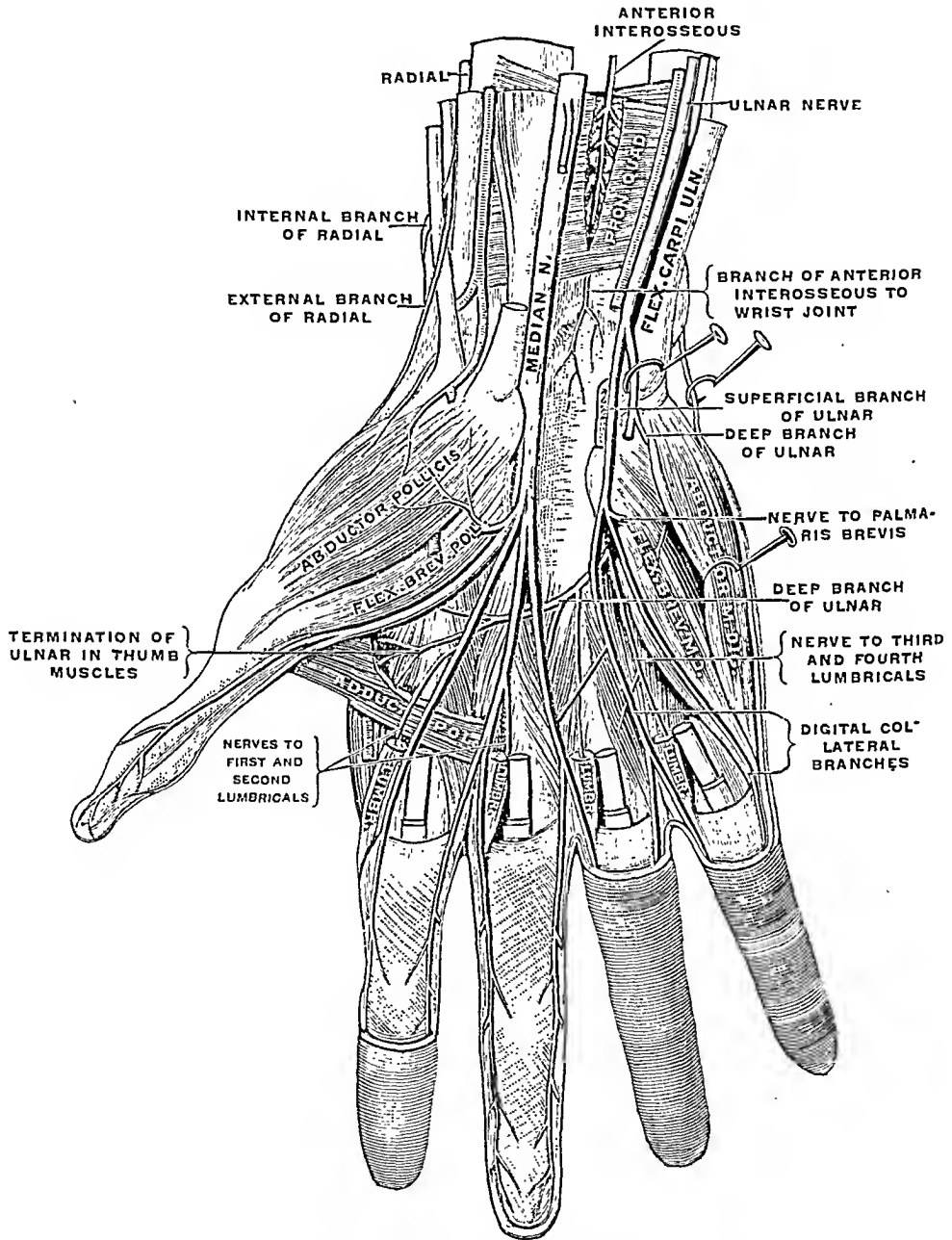


FIG. 2 (Testut's Anatomy).—Showing the branches of the ulnar and median nerves after removal of the annular ligament.

The *motor types* of neural atrophy of the hand are characterized by an absence of objective sensory symptoms, and occur as two distinct clinical types—a *hypothenar type*, dependent upon a com-

pression neuritis of the deep palmar branch of the ulnar nerve, and a *thenar type*, dependent upon a compression neuritis of the thenar branch of the median nerve. Both nerves are purely motor in character, and together supply the entire musculature of the hand, with the exception of a small subcutaneous muscle, the palmaris brevis, which is innervated by a branch from the superficial palmar division of the ulnar nerve.

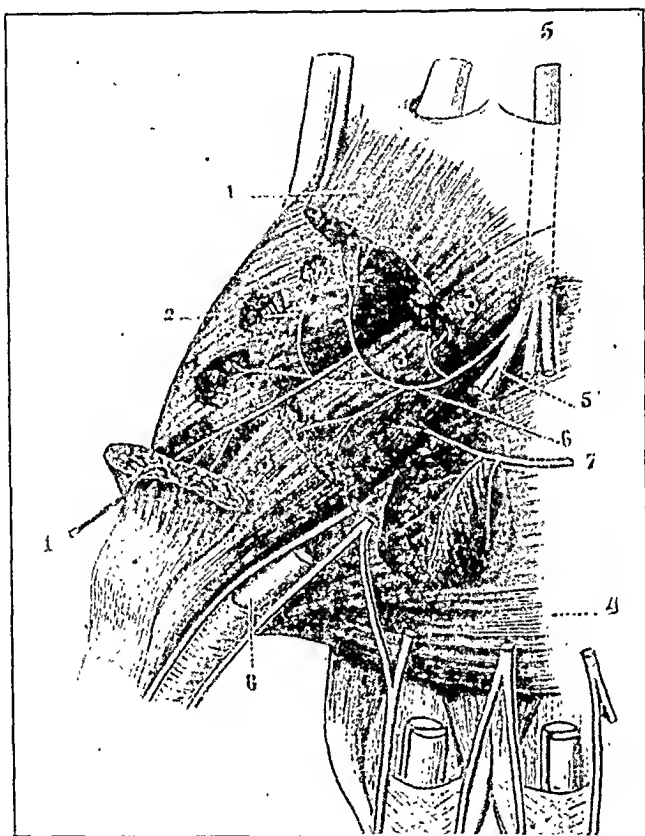


FIG. 3 (Testut's Anatomy).—Showing the motor branches of the thenar eminences: 1, abductor brevis pollicis; 2, the opponens pollicis; 3, 3', superficial and deep heads of the flexor brevis pollicis; 4, adductor pollicis; 5, median nerve with, 5', terminal branches; 6, nerve to the thenar muscles (thenar branch); 7, termination of the deep branch of the ulnar in the adductor pollicis and the deep head of flexor brevis pollicis.

The paralysis of the *hypothenar type* is limited to the distribution of the ulnar nerve, and of the *thenar type* to that of the median nerve, and are accompanied by atrophy and the electrical reactions of degeneration in their respective distributions.

ANATOMICAL CONSIDERATIONS. All the small muscles of the hand are supplied by either the median or the ulnar nerve. The median, through its *thenar* branch, innervates the abductor pollicis, the opponens pollicis, and the outer head of the flexor brevis pollicis. These muscles compose the outer portion of the thenar eminence;

in addition, the first and second lumbricales are usually supplied by the median nerve (Figs. 1 and 3). The thenar branch is purely motor, and leaves the main trunk as it emerges from beneath the anterior annular ligaments of the wrist; it then turns back over the edge of this tendinous membrane, and passes toward the thenar eminence. The compression of the nerve, I believe, takes place as it passes over the annular ligament (Figs. 1 and 2).

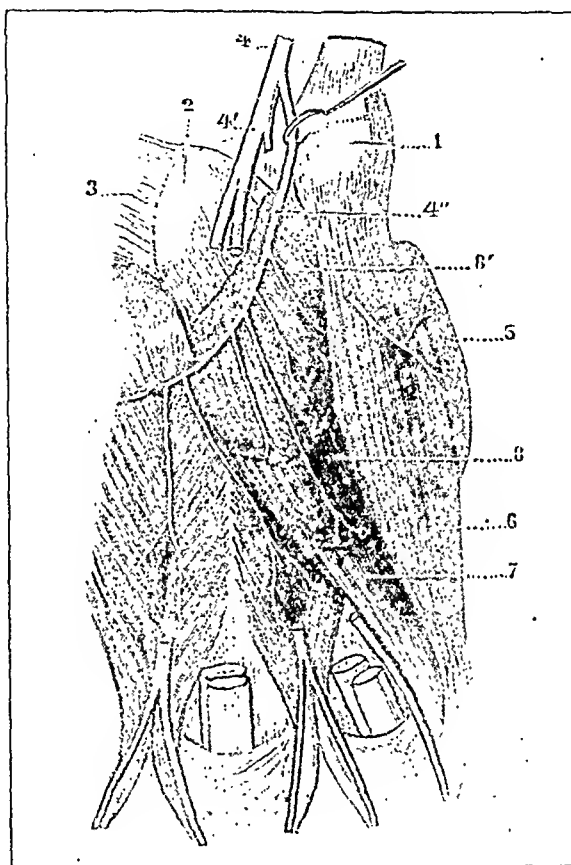


FIG. 4 (Testut's Anatomy).—Showing the deep palmar branch of the ulnar nerve and its relations to the tendinous origin of the abductor minimi digiti and the flexor brevis minimi digiti: 1, pisiform bone; 2, unciform process of the unciform; 3, anterior annular ligament; 4, ulnar nerve; 4', superficial palmar branch; 4'', deep palmar branch; 5, palmaris brevis; 6, abductor minimi digiti; 7, flexor brevis minimi digiti; 8, 8', opponens minimi digiti.

All the remaining intrinsic muscles of the hand are supplied by the ulnar. This nerve, just above the level of the pisiform bone, divides into two terminal branches—the *superficial palmar*, which is sensory, and the *deep palmar*, which is purely motor. The deep palmar branch innervates all the muscles of the hypothenar eminence, the palmar and dorsal interossei, and the third and fourth lumbricales. Soon after its origin, the deep palmar passes between the tendinous origins of the abductor minimi digiti and the flexor

brevis minimi digiti, in a downward, backward, and outward direction, winding in its course beneath the hook of the unciform bone, at which point it breaks up into its terminal muscular branches. Occasionally it pierces the tendon of the flexor brevis minimi digiti (Figs. 2 and 4).

In the *hypothenar type* of neural atrophy the nerve is, I believe, compressed at this point; that is, after giving off of its superficial sensory branch and before breaking up into its muscular terminals. As I have already indicated, the palmaris brevis is supplied by a small muscular branch arising from the superficial palmar, so that the function of this muscle would be preserved.

The intrinsic muscles of the hand are therefore supplied by two distinct nerve trunks, both of which are purely motor in character, the one arising from the median and the other from the ulnar nerve. Both of these branches, soon after leaving the trunk of the nerve, are in close relation with tendinous structures, so that when subjected to prolonged or unusual compression, as would occur in certain occupations, they would be exposed to the dangers of injury with consecutive degeneration of the nerve and atrophy of the corresponding muscles.

A Case of Occupation Neuritis of the Deep Palmar Branch of the Ulnar Nerve (Hypothenar Type of Neural Atrophy of the Hand).

J. R., single, aged forty-seven years, has been an oyster opener by occupation for many years, having opened on an average from four to five thousand oysters a day. He has always indulged freely in alcohol, and more especially during the past year. He has had gonorrhœa several times, and a chancroid at the age of seventeen. He denies lues. In opening the oysters he uses the usual oyster knife, having a heavy metal handle and a short blade. The knife handle rests in the hollow of the hand, and is grasped firmly by the fingers, more especially by the little and the ring fingers; the thumb being pressed against the opposite side of the handle, in this way making the grasp firm and guiding the direction of the blade. So that in using this knife, the act consists chiefly in flexion of the fingers, more especially of the little and ring fingers, with an opposing movement of the thumb; the handle is not pressed against the hypothenar region with any degree of power.

ONSET. Three months before coming under my observation he noticed while working that he experienced considerable difficulty and awkwardness in handling the knife. The following day his hand was no better, and he was forced to abandon his occupation. Since that time he has been unable to resume work. He experienced no pain in the hand whatever, and at no time were there any paræsthetic disturbances in the fingers.

PRESENT CONDITION. The patient is a short, somewhat corpulent, and very muscular man. The general physical and neurological examination is negative. On extending, or attempting to extend, the fingers of the right hand, there develops a slight tremor, which is not present on the left. The fingers cannot be completely extended, but are held in a somewhat flexed position, which is more apparent in the little and the ring fingers. Both the little and the index fingers are held somewhat abducted, while the middle and ring fingers remain in close apposition. There are evident signs of muscular atrophy in the intrinsic muscles of the hand, and the hypothenar eminence feels soft and flabby. No fibrillary twitchings are visible. He is unable to separate or approximate the fingers. Adduction of the thumb is possible, but with much less force than on the left side. He is also unable completely to extend the middle and distal phalanges, or to flex the basal phalanges while holding the fingers extended. No voluntary movements are possible in any of the muscles of the hypothenar eminence, *with the exception of the palmaris brevis muscle*, which produces the typical creasing of the skin over the hypothenar region. The movements of the thumb are, on the contrary, quite free and active, and there is very good power of abduction and apposition. Flexion of the basal phalanx of the thumb and adduction are distinctly paretic.

There is normal power in the extensors and flexors of the wrist, and in the long flexors and extensors of the fingers. I would especially emphasize the preservation of the ulnar flexion of the wrist and the long flexors of the fingers supplied by the ulnar nerve. The muscles of the upper arm and shoulder are normal.

The tendon reflexes of both upper and lower extremities are normal. There is no tenderness of the nerve trunks or of the muscular tissues of the right arm and hand. The skin of the right arm, hand, and fingers shows absolutely no impairment of sensation to touch, pain, or temperature. The deep sensibility of the fingers is preserved, and the stereognostic sense is unimpaired.

Electrical Reactions. The muscles of the upper arm and forearm react normally to both currents. Strong faradic and galvanic currents passed through the ulnar nerve in the groove at the elbow produce flexion movements of the wrist and fingers on the ulnar side, but no response in the intrinsic muscles of the hand. Currents passed through the median nerve at the bend of the elbow and in the forearm produce distinct contraction in the muscles of the thenar eminence. Strong faradic currents applied directly to the muscle fail to elicit any response in the muscles of the hypothenar eminence or the interossei. A good response, however, is obtained in the muscles of the thenar eminence. The direct galvanic current produces in the muscles of the hypothenar and interossei a slow vermicular response with definite polar changes. In the thenar

eminence a normal galvanic response is elicited over the area of the abductor and opponens pollicis. If stronger currents are used, and if the electrode is placed over the eminence toward the ulnar side of the hand, a mixed normal and degenerative reaction ensues, evidently from diffusion of the currents to the deeper muscles of the thenar region which are degenerated.

REMARKS. The case just described presents a paralysis of all the intrinsic muscles of the hand supplied by the ulnar nerve, with evidences of atrophy. The reactions of degeneration are complete. Sensation over the ulnar distribution is normal, and at no time was pain or paresthesias experienced in this area. Furthermore, the small muscle group of the thenar eminence supplied by the median nerve was normal in its function and electrical responses. The man had been an oyster opener since his boyhood, and had never previously experienced any difficulty of this nature. He was, in addition, addicted to alcohol, which had been excessive during the last year, so that aside from occupation as a factor, a toxic element must also be considered (toxico-professional palsy). In using the oyster knife the heavy handle did not impinge on the base of the hypothenar region, so that direct pressure upon the nerve trunk may be excluded. It was held chiefly in the grasp of the fingers, more especially of the little and ring fingers, assisted by the opposing movements of the thumb. Flexion of the basal phalanx of the little finger brings into action both the abductor and flexor brevis minimi digiti, which would cause a compression of the nerve as it passes between the tendinous origin of these two muscles. I would particularly emphasize the preservation of the palmaris brevis muscle, which receives its innervation through the superficial palmar, which is additional clinical proof in favor of placing the site of the compression in the deep volar branch.

In my original paper on this subject,¹ three cases were recorded associated with the following occupations: That of jeweller, brass polisher, and machinist. A summary of the clinical pictures is briefly as follows (Fig. 5): The palsy developed without the accompaniment of pains, paresthesias, or anesthetics in the ulnar nerve distribution. On holding out the affected hand the fingers could not be completely extended, a slight flexion persisting in all, but more especially in the little and ring fingers. The index and little fingers are held somewhat abducted, while the middle and ring fingers remain in close apposition; there is a loss of spreading and approximation movements of the fingers, of flexion of the basal phalanges, and of extension of the middle and distal phalanges. Adduction of the thumb is also lost or very much diminished.

¹ Occupation Neuritis of the Deep Palmar Branch of the Ulnar Nerve, Jour. of Nerv. and Ment. Dis., 1909.

Flexion of the basal phalanx of the thumb is weakened; abduction and apposition of the little finger are abolished. In brief, an ulnar paralysis, limited to its distribution in the hand. With the paralysis there is more or less atrophy of the muscles, and electrical reactions of degeneration are present. In all of the cases there was a considerable impairment of the more delicate functions of the hand, and the occupation instrumental in producing the palsy had to be abandoned.

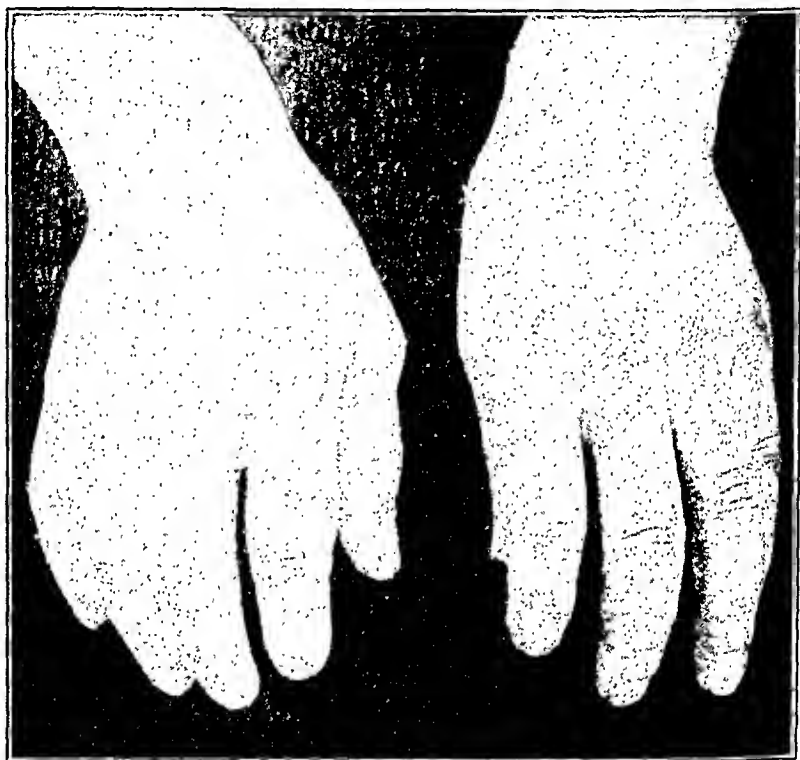


FIG. 5.—Occupation neuritis of the deep palmar branch of the ulnar nerve, occurring in a jeweller, with atrophic paralysis of the intrinsic muscles of the left hand supplied by the ulnar nerve. Complete reactions of degeneration. No objective sensory disturbances.

With the preservation of the long flexors and extensors of the wrist and fingers, and the muscles of the thenar eminence supplied by the median nerve, there still remained a considerable degree of power and variety of movement in the hand. This paralysis without sensory disturbances I attributed to a compression neuritis of the deep volar branch of the ulnar, as it passes between the tendinous origin of the muscles of the hypothenar region (Figs. 2 and 4).

In all of the cases in which this form of paralysis occurred the occupation was one requiring flexion movement of the fingers, more especially of the basal phalanges. When the basal phalanx of the little finger is flexed, both the abductor and the short flexor

are put in action, and as the short abductor takes its origin from the pisiform bone, and the short flexor from the hook of the unciform, the deep volar branch separating them at their points of origin, persistent and long-continued flexion of these muscles would seriously expose this nerve to the dangers of muscular compression. The possibility of traction must also be considered from the relation it bears to the hook of the unciform.

Cases of Compression Neuritis of the Thenar Branch of the Median Nerve (Thenar Type of Neural Atrophy of the Hand).

CASE I.² (Neurological Clinic of the Cornell Medical School).—E. G., aged fifty years; engaged in the occupation of folding and sealing newspapers, for mailing purposes, during the last thirty years. He works in all about seven hours a day. During this time he folds and sorts heavy sheets of paper, which bring into play chiefly the thumb and fingers. After the packages are sealed they are carried and deposited in a convenient place, which throws a considerable strain on the arms and shoulders. Occasionally during the last nine years, after an unusual stress of work, he has experienced a general numb, tired feeling in the arms and shoulders, and at times the fingers felt numb and would tingle, but this would soon pass off with rest and never lasted more than an hour or so. At times he also has a cramp-like sensation in the right hand, especially the thumb. This also was very transient in nature. In folding the heavy sheets of paper the strain is largely caused by the pressure of the thumb against the roll, more particularly of the right hand. About two years ago, he first noticed a slight wasting of the muscle along the radial side of the thenar eminence. This area was small at first, but gradually increased in size, up to a certain point, and has remained stationary ever since. During this time he continued his occupation, saving the right hand as much as possible, which threw an unusual amount of strain on the left. Of late, he finds that the left hand is also becoming affected in a similar manner.

PRESENT CONDITION. The general neurological examination is negative. The heart, lungs, and kidneys present no symptom of disease. Both upper extremities are well developed and present no diminution in the gross motor power, with the exception of the movements of the thumb on the right side, and to a less extent on the left. There are no fibrillary twitchings, and the biceps, triceps, and supinator reflexes are present.

There is in the right thenar region a sharply defined atrophy, which extends along the outer side of the eminence. This presents

² Presented at a meeting of the New York Neurological Society, November, 1909.

a rather deep depression, as if the muscular tissue had been scooped out (Fig. 6).

Over the left thenar eminence a slight flattening is perceptible along the metacarpal bone, and the muscular tissue is soft and doughy. There is, however, no well-marked atrophy. The other intrinsic muscles of the hand, the hypothenar and the interossei, present no signs of atrophy and no diminution in their motor power. The sensation of both upper extremities is unimpaired, and very careful tests of the tactile, pain, and thermic sensibility of the hands show no objective impairment in either the ulnar or median distribution. The dynamometer on the right hand registers 38, and on the left, 41.

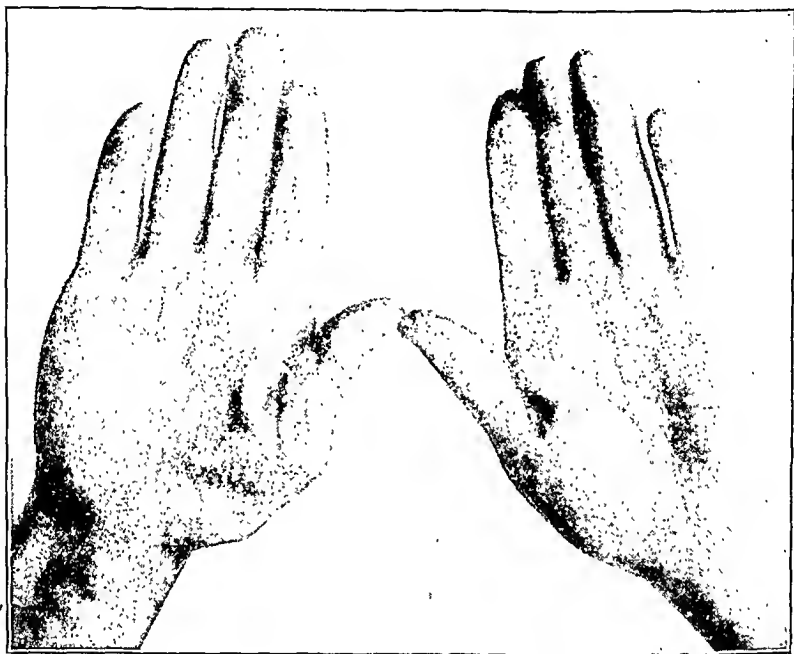


FIG. 6.—Occupation neuritis of the thenar branch of the median nerve, showing a circumscribed atrophy of the right thenar eminence which contains a remnant of muscular tissue showing the reactions of degeneration; the sensations are normal. A scarcely perceptible flattening of the left thenar, with complete reactions of degeneration in the abductor and opponens pollicis is present.

Electrical Reactions. Electrical examination of the upper extremities shows normal reaction in all the muscles, with the exception of those composing the thenar eminence in the distribution of the median nerve. An indirect faradic or galvanic current passed through the median nerve at the bend of the elbow, fails to produce any response in the corresponding muscles of the thenar region on either the right or the left side. Faradic currents directly applied to the right thenar fail to produce a reaction in either the abductor or opponens pollicis. Strong galvanic currents applied directly to the right thenar region over the atrophic area produce a slight vermicular response in a small muscle remnant. Direct

faradic excitation of the left thenar eminence fails to elicit any response in the abductor pollicis or opponens pollicis. The galvanic current produces a typical slow vermicular reaction in these muscles, with reversal of the poles.

The patient was advised to give up his occupation, and electrical treatment has been systematically carried out. On November 22, 1908, the atrophy of the right thenar eminence was the same as on the first examination. There was also present a slight but definite flattening over the left thenar region, as was previously noted. The electrical changes were practically the same as on the first examination; that is, no response in the right thenar over the atrophic

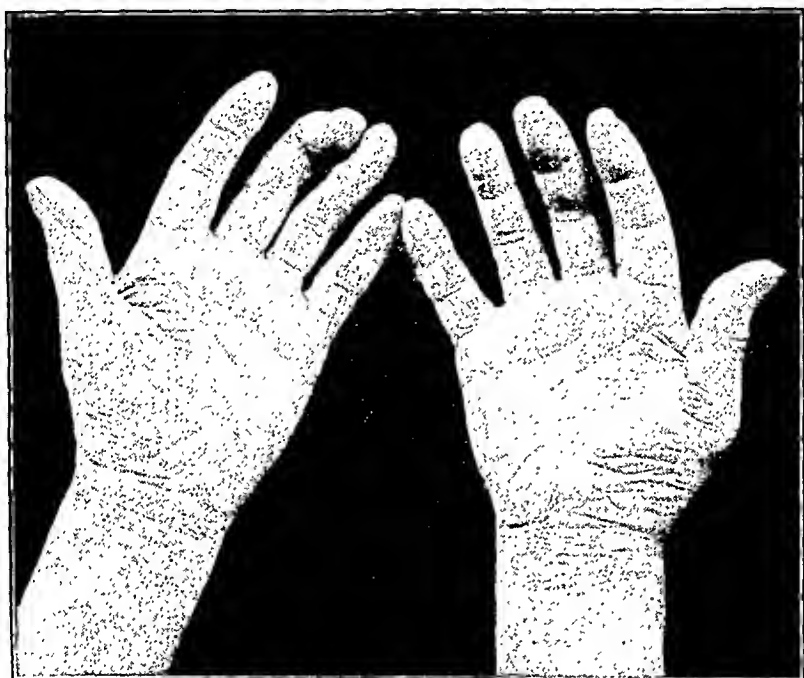


FIG. 7.—Photograph of same case as Fig. 6, taken one year later. The atrophy of the right thenar is less marked, and there is still slight flattening apparent over the left thenar, with reactions of degeneration. No sensory disturbances.

area excepting to strong galvanic currents, which elicited a vermicular response in a persisting muscle remnant, of which the anodal closing contraction was greater than the cathodal closing contraction. In the left thenar region the abductor pollicis and opponens pollicis showed complete reactions of degeneration. There was an absence of pains, paresthesias, or objective sensory disturbances in the hands or fingers; no fibrillary twitchings and no evidence of atrophy in the small muscles of the hand supplied by the ulnar nerve.

June 1, 1909. Patient complains occasionally of dull aching pain in the right metacarpal joint, both at its articulation at the wrist and with the thumb. These seem to change with the weather. He has no paresthesias and no objective sensory disturbances in the median or ulnar distribution. At times he has an aching pain

in the left thenar region, which is dull in character. The flattening along the left thenar eminence is less marked, and the atrophic excavation of the right thenar is less sharply defined (Fig. 7). Electrically there is no faradic response in the abductor or opponens pollicis on either side. The left thenar still shows sluggish galvanic responses with reversal of the poles, and in the right no reaction at all is elicitable, save for the small muscle remnant previously noted.

CASE II. (Referred by Dr. Isadore Abrahamson, of New York).—Patient is a woman, aged sixty-nine years, married, and has two children; a housewife by occupation. When about fifty years of age she did considerable ironing, working many hours each day. In using the irons she held the thumb well under the handle, so that there was no direct pressure upon the thenar eminence. She, however, grasped the handle firmly, which would bring into play the small muscles of the thumb. A little later she first noticed a slight wasting of the right thenar region along its radial side, which gradually increased in size. A year later a similar condition developed in the thenar region of the left hand, likewise along its radial border. These areas of atrophy have persisted up to the present time and have remained stationary. She never gave up ironing, but did less as she grew older. At the time of the onset she had a numb feeling in the extreme tips of all the fingers of both hands. This, however, was not permanent, and would come and go. It was not confined to the median distribution, and was more in the nature of an acroparesthesia.

PRESENT CONDITION. April 28, 1909. The patient has a typical *thenar atrophy* on both sides, more marked upon the right than on the left. There are no fibrillary twitchings, and no atrophy or weakness in the other muscle groups of the hands or arms. The arm-jerks are present, and the *objective sensation is perfectly normal*. There is not the slightest trace of any disturbance of the touch, pain, or temperature sensibility in either the ulnar or the median distribution of the hand.

Electrical Examination. There is no faradic response, either direct or indirect, in the abductor pollicis or opponens pollicis on the right or left side, nor can these muscles be contracted through the median nerve by strong galvanic currents. The direct galvanic current applied to the right thenar eminence, where the atrophy is more marked, elicits no response whatever. In the left hand, however, a slow vermicular reaction is produced in the atrophic area, the anodal closure contraction being greater than the cathodal closure contraction.

CASE III. (Verbal communication by Dr. H. M. Moyer).—Following the discussion of my paper,³ which was read at a meeting

³ Occupation Neuritis of the Thenar Branch of the Median Nerve: A well-defined Type of Clinical Atrophy of the Hand. Trans. Amer. Neurological Association, 1909.

of the American Neurological Association in May, 1909, one of the members communicated to me, a personal experience with thenar atrophy. This had come on after a long bicycle ride, during which he had used hard grips on the handle bars. A few days later he noticed fibrillation and waving of the muscular tissue along the radial side of the right thenar eminence. This was followed in the course of a week or two by distinct wasting of the muscles, which corresponded exactly to the distribution of the thenar branch of the median nerve, as shown in Fig. 6. With the appearance of atrophy, the fibrillary waves ceased and did not recur subsequently.

At no time were pain, subjective or objective disturbances of sensation in the hand noted. Some of his colleagues suggested the pleasing possibility of progressive muscular atrophy, but in the course of a few months the scooped out, atrophic depression of the thenar region began to fill in, and at present no difference in the volume of the two sides is apparent.

REMARKS. The thenar type of neural atrophy of the hand is readily recognized by the characteristic limitation of the atrophy to the abductor pollicis, the opponens pollicis, and the outer head of the flexor brevis pollicis, all of which are supplied by the thenar branch of the median nerve. As the atrophic area is situated between the first metacarpal bone externally and the body of the inner portion of the flexor brevis pollicis, a sharply demarcated depression results, as if the muscular tissue had been scooped out.

The electrical reactions vary with the stage and the degree of the atrophic process, and are characteristically neural. Objective disturbances of sensation in the distribution of the median nerve were absent in all of the cases, so that the thenar filaments must have been injured after leaving the main trunk of the median (Figs. 1 and 2).

It will be recalled, from the anatomical descriptions, that immediately after leaving the main trunk the thenar branch stands in immediate relationship to the palmar border of the anterior annular ligament, beneath which it emerges and over which it passes in a backward and outward direction to its destination in the muscles of the thenar region. The injury to the nerve, therefore, must take place at this point, induced by the continuous or frequently recurring pressure of muscular action.

The general usefulness of the hand is not greatly impaired in this type of neural atrophy, except for finer movements, in which the thumb plays an important role, as, for instance, in writing.

The first metacarpophalangeal joint may also be considerably weakened and relaxed as a result of the atrophy.

Because of the comparatively slight disturbance of the general power and utility of the hand, the occupation which was instrumental in the production of the paralysis is sometimes persisted in, and under these circumstances the atrophy may become perma-

ment, as in Case II and probably in Case I, although here a slight improvement was apparent after electrical treatment for one year. In Case III the complete restoration of muscular tissue and function is to be attributed to the prompt recognition of the etiological factor and its removal.

The prognosis in these cases may therefore be regarded as favorable, if the causative factor is discovered at an early stage and proper precautionary measures and treatment are instituted. In the literature of professional palsies and atrophy of the hand, cases are cited in which there was an atrophy of the thenar eminence, usually, however, in conjunction with other of the small muscles of the hand, or with sensory disturbances in the median distribution.

I am aware of no reported cases in which the atrophy has been shown to be limited to the thenar distribution of the median nerve. as in the group of cases just described, the clinical importance of which is dependent upon their resemblance to the hand atrophy of spinal origin.

DIAGNOSIS. The *neural types* of atrophy of the hand muscles are readily separated from those of myelopathic and myopathic origin by the strict limitation of the paralysis to the distributions of the ulnar and the median nerves and by the degenerative character of the electrical reactions.

The absence of sensory disturbances serves to separate them from the atrophy which follows lesions and compressions of the ulnar and median nerves higher up, that is, above the origin of the deep palmar and thenar (motor) branches.

In the *thenar* and *hypothelar types* of neural atrophy the distribution of the palsy and accompanying atrophy are the same as after other lesions of the median and ulnar nerves, the degree of the atrophy depending upon the severity and duration of the palsy.

In none of the cases were fibrillary twitchings present in the affected muscles, with the exception of one case only, in which fibrillary waves were noted at the time of onset, but ceased with the appearance of atrophy, and did not recur subsequently. In reaching a diagnosis, I would emphasize the importance of demonstrating the limitation of the paralysis, atrophy, and degenerative reactions to the motor distribution of the ulnar or median nerves, as the case may be. This neural limitation of the palsy may be overlooked unless special care is exercised, as there are no sensory symptoms to suggest the nerve distribution. In the *hypothelar type* there is some atrophy of the muscles which go to form the thenar eminence, that is, the adductor pollicis and the inner head of the flexor brevis pollicis, which are supplied by the ulnar nerve. This produces some flattening and atrophy in the thenar region, and might simulate involvement of the median nerve on superficial examination. Still greater care must be exercised in interpreting the electrical reactions in the thenar type of atrophy. The

diffusion of currents to a part of the flexor brevis pollicis and the adductor pollicis, both of which are supplied by the ulnar nerve, may give the impression of a positive reaction of degeneration in the thenar region, and yet the muscles supplied by the thenar branch of the median nerve may be perfectly normal.

I would also recall a type of occupation atrophy of the hand described by Gessler,⁴ which bears some resemblance to the hypothernar type of neural atrophy. This question I have already discussed at some length in a previous communication.⁵ Gessler⁶ regarded the underlying lesion in his cases as a degeneration of the motor end-plates and intermuscular nerve terminals, induced by prolonged and persistent muscular contractions with insufficient muscular relaxation, this producing an anemia of the parts, with consecutive degenerations of these delicate neural structures. As a basis for this theory he presented the results of some experimental studies in warm- and cold-blooded animals in which such lesions were produced. In my opinion, Gessler's views require further clinical confirmation before they are accepted as the pathological basis for a group of professional muscular atrophies. The class of cases which I describe are, however, readily separated by the strict limitation of the atrophic palsy to the distribution of either the median or ulnar nerves.

A Case of Progressive Muscular Atrophy, Resembling the Thenar Type of Neural Atrophy (Fig. 8).

The following case is recorded as showing the rather close resemblance which may exist between the spinal and the neural atrophy of the hand.

The patient, a woman, unmarried, aged forty-two years, was admitted to the Cornell Clinic, March 22, 1910. Since her eighteenth year she has been a victim of epilepsy. She is a waitress and helper in a hotel; there is nothing exceptional in her occupation, which is more or less general in character, except that three times each day she slices bread for the entire establishment, which requires constant cutting for about twenty minutes. For this purpose a large bread knife is employed, which is grasped firmly by the right hand. There is no history of venereal disease or of alcoholic excesses. One year ago she passed through an attack of subacute articular rheumatism, lasting about seven weeks.

Her present trouble dates from June, 1909, when she first noticed a slight weakness of the right hand, and about the same time a

⁴ Die motorische Endplatte und ihre Bedeutung für die peripherische Lähmung, Habilitationsschrift, München, 1885.

⁵ Jour. Nervous and Mental Disease, 1909.

⁶ Eine Eigenartige Form von progressiver Muskelatrophie. Med. Correspondenzbl., 1896, 281.

flattening and wasting of the ball of the right thumb, both of which have gradually grown worse. There has been no pain in the hand at any time and no paresthesia.

Examination. There is a well-marked atrophy of the right thenar eminence along its radial side (Fig. 8). There is also a slight, scarcely perceptible thinning of the muscles of the third and fourth interosseous spaces and of the hypothenar region. Fibrillary twitchings were not demonstrable at first, but subsequent examina-

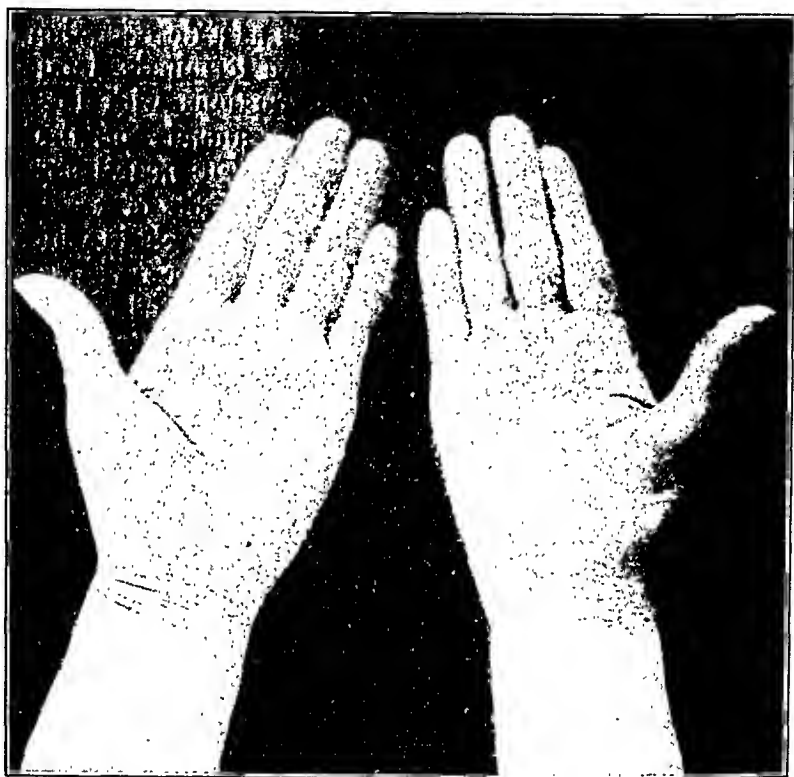


FIG. 8.—A case of early muscular atrophy of spinal origin, resembling the thenar type of neural atrophy. In addition to the wasting on the radial side of the thenar, there were atrophy and fibrillations of the interossei and slight atrophy along the ulnar side of the forearm.

tions revealed their presence in the interossei and in some of the muscles of the hypothenar. The ulnar side of the forearm is also the seat of slight wasting, there being a difference of one-half inch between the two sides. All movements of the right hand are readily performed, but are distinctly weaker than the left. The gross motor power of the other muscles of the upper extremity is undiminished.

The reflexes of the upper extremity are active on both sides, but more so on the right, where the periosteal and bone reflexes of the hand and fingers are readily elicited. Sensation is perfectly normal. The tendon reflexes of the lower extremities are present

and active, but not exaggerated. There is no Babinski phenomenon on either side.

The pupils are equal and react normally. A careful general and neurological examination failed to reveal any symptoms, other than the weakness with atrophy of the right hand, with fibrillary twitchings and exaggeration of the reflexes of the right upper extremity.

Electrical Reactions. Strong faradic and galvanic currents passed through the median nerve fail to elicit any response in the atrophic muscles of the right thenar eminence. A strong faradic current applied directly to the thenar eminence produces a sluggish response, which apparently originated in the opponens pollicis. The direct galvanic current elicits a slow vermicular response in the thenar region, in which the A C C is $>$ K C C. The electrical response, both direct and indirect, of the other intrinsic muscles of the hand, as well as those of the forearm, are practically normal.

COMMENT. This case is interesting from a diagnostic point of view.

The atrophy is well defined in the thenar region, and at the first glance appears limited to the distribution of the thenar branch of the median nerve (Fig. 8). The completeness of the reactions of degeneration, which are confined to the muscles of the thenar region, are also very suggestive of a neural origin.

A more careful scrutiny of the case, however, shows a slight general wasting of the hypothenar, interossei, and along the ulnar side of the forearm, with fibrillations, exaggerated arm reflexes, both tendon and periosteal; so that the muscular atrophy must be interpreted as of spinal origin, an early stage of the Aran-Duchenne type.

It is, of course, not impossible that the two conditions, neural and spinal, may be present in combination, as certain occupations requiring excessive use of the hands are recognized etiological factors in both groups of cases. It is certainly singular that atrophy and reactions of degeneration should be so circumscribed to the distribution of the thenar branch in a case of progressive muscular atrophy.

CONCLUDING REMARKS. In addition to the atrophic paralyses of the intrinsic muscles of the hand, of *myelopathic* and of *myopathic* origin, I believe that a *neural* type should also be recognized. Those of neural origin may be separated into two well-defined clinical types, both due to a compression lesion of a *motor* branch of a mixed nerve. These may be appropriately designated as follows:

A *hypothenar type*, which term indicates the site of the compression at the base of the hypothenar eminence and its relationship to the ulnar nerve.

A *thenar type*, which also indicates the site of the compression at the base of the thenar eminence, and the relationship to the median nerve.

THE ASSOCIATION OF SUPPURATIVE DISEASE OF THE NASAL ACCESSORY SINUSES AND ACUTE OTITIS MEDIA IN ADULTS.

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THE subject indicated in the title of this paper is one to which I have given considerable attention for several years. The clinical study has been almost entirely on patients seen in private practice, thus affording an opportunity for a more thorough examination than can usually be given to the individual patient in a clinic.

While many of the cases of suppurative nasal accessory sinus disease are easily diagnosticated, others are only recognized after cleansing the nares, thoroughly contracting the nasal mucous membrane by cocaine and adrenalin, and observing after a lapse of a quarter of an hour or more, the escape of secretion into the nares or nasopharynx. Transillumination, in the case of the antra, and to a less extent for the frontals, is an important aid to diagnosis.

I have chosen to limit the report to adult cases, because, while suppuration in the nasal accessory sinuses undoubtedly occurs in children from the time of the earliest appearance of the sinuses up to the time of their full development, it is often very difficult to be positive of the diagnosis of sinus disease.

The factors which in children prevent our satisfactory examination are: (1) The small size of the nasal chambers; (2) the proportionately larger size of the turbinal bodies; (3) the relatively greater amount of swelling of the turbinal bodies when acutely inflamed; (4) the intractability of children to the necessary application of cocaine, and the use of instruments for probing and puncturing the cavities; and (5) transillumination in most children under twelve years of age is unreliable or positively misleading. The two antra develop so unevenly that one may be much darker than the other, and yet, if the darker one is washed out, no secretion is found in it.

It seems best to divide the subject into two parts: (I) Statistics, and (II) Personal impressions.

I. STATISTICS. I have analyzed the histories of all *new* patients seen between October 1, 1909, and March 1, 1910, who came to me suffering from acute suppurative otitis media, acute rhinitis, acute sinusitis (using this term to indicate suppuration of one or more of the nasal accessory sinuses), and chronic sinusitis.

There were 16 cases of acute suppurative otitis media; 26 cases of acute rhinitis, without sinus involvement; 31 cases of acute sinusitis (all of which also had an acute rhinitis); and 36 cases of chronic sinusitis.

I shall study these cases from an otological and a rhinological standpoint.

Otological Standpoint. The 16 cases of acute suppurative otitis media sought relief of the earache, and regarded the accompanying "cold in the head" as of little moment. The examination of the fundus revealed a red and bulging membrana tympani. A spontaneous perforation had occurred in 3 cases. In all 16 the operation of myringotomy was performed, usually after inducing nitrous oxide anesthesia. In 3 of the 16 cases, 19 per cent., a thorough examination of the nares and sinuses showed only an acute rhinitis, with no involvement of any of the sinuses. All 3 made an uneventful recovery.

Of the 13 remaining cases, all had an acute rhinitis complicated by acute sinus disease; that is, 81 per cent. of this series of acute otitis media had at the time of their first visit, and antedating the onset of the aural disease, a suppuration in the nasal accessory sinuses. Of these cases, 8 made an uneventful recovery for ears and sinus disease, while in 5, or 39 per cent., the disease extended to and involved the mastoid to such an extent that a mastoid operation was performed.

In 1 case, a nurse, Miss C., had acute rhinitis, complicated by right antrum disease, four days before pain in the ear began. The pain in the ear commenced at 6 P.M. At 8.30 P.M., under nitrous oxide anesthesia, myringotomy was done. A smear at the time of operation revealed the pneumococcus. On the second day, there was a profuse bloody discharge and mastoid tenderness; on the third day the mastoid tenderness had increased with considerable prolapse of the posterior-superior wall; on the fourth day the tenderness of the mastoid increased with œdema of the skin over the mastoid, and the prolapse was more marked. As there were no facilities for operating on the mastoid or caring for the patient in the Nurses' Home, she was sent to the New York Eye and Ear Infirmary, where Dr. E. B. Dench exenterated the mastoid. The patient made an excellent recovery.

One of the cases, a nurse, Miss B., had influenza, diphtheria, and an acute pansinusitis. Both mastoids were involved, and operated on by my associate, Dr. H. M. Taylor.

Another mastoid case, Mrs. R., had suppuration in the left frontal, ethmoid, and antrum, and probably also the left sphenoid; but a septum, enormously deflected to the left, prevented examination of the left sphenoid. The left mastoid and sinuses healed.

Miss S. had the right frontal, ethmoid, antrum, and sphenoid involved. The right mastoid was operated on and recovery ensued.

Another patient, Mr. M., had the right antrum alone involved. The right mastoid was operated on and recovery followed.

A very interesting clinical fact in this series of mastoid cases is that the infection of the tympanum and mastoid was limited to the

same side as that of the nasal accessory sinus disease. In the bilateral mastoid case there was a bilateral nasal involvement.

Of the 8 uncomplicated cases of otitis media, *all* had pus in the antrum of the corresponding side. Three also had pus in the frontals of the same side, and 2 had pansinusitis. Three other patients sought relief from a severe earache. The pain was referred to the auditory canal and mastoid region. In 2 of the cases the pain was unilateral, in 1 bilateral. In all of these cases the fundus and canal were normal. The slightest touch of the skin over the mastoid proved exquisitely tender. They were typical cases of otalgia. In one case the antrum on the painful side was filled with pus. A few irrigations of the antrum cured it and the otalgia. In the bilateral otalgia case there was a chronic pansinusitis. On establishing good drainage from the sinuses, the otalgia disappeared. The third case had a chronic suppuration in the sphenoid and posterior ethmoid of the otalgic side. She still has exacerbations and remissions of her sinus disease, and *pari passu*, of the otalgia.

Rhinological Standpoint. There were 26 cases of acute rhinitis. In order that there may be no misunderstanding about these cases, I wish to state that it is unusual for me to see the milder forms of this disease. Most of the cases are accompanied by hypervascularization of the tissues and considerable hypersecretion, the character varying from watery to mucopurulent, according to the stage of the disease. It is often difficult to be certain that there is not some slight involvement of the sinuses. If either antrum on transillumination was darker than the other, it was irrigated.

Of these 26 cases, 23 did not have acute ear symptoms or signs other than a feeling of stuffiness from tubal congestion, and a slight dilatation of the vessels of the tympanic membrane. Three of the 26, or 11.5 per cent., had acute suppurative otitis media. I have been unable to find in rhinological or otological literature any figures for comparison by which to judge whether this percentage of aural complication is high or low.

Acute Sinusitis. There were 31 cases of acute sinusitis. Thirteen of these cases (42 per cent.) had an acute suppurative otitis media as a complication at the time they came under observation. The ears were treated as heretofore described. The treatment of the sinus disease consisted in contracting the nares with a 2 per cent. solution of cocaine, waiting for ten minutes or longer, until by inspection the swelling of the nasal mucous membrane had subsided, and gentle irrigation of each naris, by means of a syringe containing a warm (temperature, 110° F.) normal saline solution, to which 0.3 per cent. of bicarbonate of sodium was added; and further cocainezation beneath the inferior turbinate, and irrigation of one or both antra through a Myles cannula passed through the nasal wall beneath the inferior turbinate into the antrum. If the frontal sinus did not

drain satisfactorily, the anterior end of the middle turbinate was amputated. The sphenoid was irrigated by means of a cannula inserted into the cavity through the ostium.

Of the 18 sinus cases not complicated by otitis media when first seen, there was but 1 case which subsequently developed an otitis media demanding operation.

H. S. S., Jr., had a slight intermittent earache for forty-eight hours, for which I was consulted. The right fundus was red with only a slight bulging of Schrapnell's membrane, and hearing was slightly impaired. The left fundus was normal. He had a pansinusitis. I did not perform myringotomy, regarding it as a catarrhal condition which might resolve without operative interference. The nares were irrigated twice daily and the maxillary sinus daily or every second day for a couple of weeks. At the end of that time the fundus had nearly returned to normal, the hearing was normal, and the acute rhinitis and sinuses practically well. He was exposed to some fresh infection (possibly a mild scarlatina), his sinuses discharged worse than ever, and there was pronounced redness and bulging of the right membrana tympani requiring a myringotomy, which was performed by Dr. McKernon.

In none of the other 17 cases, although their nares were repeatedly carefully syringed, did any aural complication develop.

I believe that the aural complication in that one case was the result of the new infection rather than any fault in the technique of irrigation.

In the 13 cases associated with otitis media the treatment of the nasal sinuses was conducted as described for the uncomplicated cases.

Chronic Sinusitis. There were 36 cases of chronic sinusitis. The duration of the disease varied from two years to twenty or more. In 4 cases the disease was limited to one antrum; in 1 case to the sphenoid and posterior ethmoid of one side; in 16 cases there was a unilateral involvement of all the sinuses, and in 15 cases, a bilateral involvement of all the sinuses. Although all of these cases were under treatment by syringing, various intranasal operations, etc., for some weeks, but 1 case developed acute otitis media.

That patient, Miss N., had pansinusitis; she gave a history of having had otitis media before coming to me. Both antra had been widely opened intranasally. A date was set for an external operation on the frontals. On the morning of that day she came to the office with a spontaneous rupture of the right membrana tympani and a purulent discharge. The sinus operation was postponed until the otitis disappeared.

In this series, 1 case in 36 (about 3 per cent.) developed acute otitis media.

To recapitulate: 81 per cent. of acute otitis media cases had sinus disease; 11.5 per cent. of acute rhinitis cases had acute suppurative

otitis media; 42 per cent. of acute sinusitis cases had acute suppurative otitis media; and 3 per cent. of chronic sinusitis cases had acute suppurative otitis media.

II. PERSONAL IMPRESSIONS. The clinician gradually accumulates an experience which is invaluable in forming his judgment as to diagnosis and treatment. While the foregoing statistics cover too short a period and too few a number of cases to be accepted as final, I wish to add some observations which I feel sure will be concurred in by other clinicians since attention is called to them:

1. Otologists agree that the infection in a large percentage of cases of acute otitis media proceeds through the Eustachian tube, complicating acute rhinitis and acute nasopharyngitis. I believe that the severer types of acute rhinitis accompanied by acute infection of the nasal accessory sinuses are far more apt to be complicated by aural disease than the milder types of acute rhinitis.

2. It is extremely rare for a patient with acute sinus disease, coming to us in the early stages, before acute otitis media has developed, to develop subsequently, during the course of the treatment, acute otitis media.

3. I am convinced that the early recognition of acute sinus disease, and appropriate treatment for its relief, will prevent many a patient from developing acute otitis media.

4. The fact that acute otitis media usually occurs on the same side as the sinus disease inclines me to the belief that the pus from the various sinuses bathes the pharyngeal orifice of the Eustachian tube and is thence forced into and infects the tympanum.

5. Cases of acute otitis media, associated with nasal accessory sinus disease, are more likely to develop such a degree of mastoiditis as to require a mastoid operation than otitis cases not complicated by nasal accessory sinusitis. One explanation of this may be in the more severe character of the infection. I am inclined to believe, however, that some patients would repair the damage to the tympanum and mastoid if relieved of the added burden of the nasal disease. I have repeatedly seen cases of severe otitis media and mastoiditis, with all the indications for mastoid operation, recover without a mastoid operation when the nasal sinusitis was recognized and treated.

6. Patients suffering from chronic suppuration in the nasal sinuses are much less prone to acute otitis media than those having acute sinusitis. In the light of modern bacteriology this may be accounted for in two ways: (a) The bacteria found in the pus in many cases of chronic sinusitis grow very poorly on any nutrient media; they seem to have lost much of their virulency. Should they be forced into the tympanum through the Eustachian tube, they may not infect the ear. (b) It is also probable that the antibodies formed in the chronic cases are a prevention against inciting a new infection. It is a well-known fact that after any operation, intranasal or external,

on a case of chronic sinusitis, the virulency of the bacteria is greatly increased, owing to the wound secretions forming an excellent nutrient medium; hence the cellulitis or erysipelas which develops after some of our external operations in cases of chronic nasal accessory sinus disease. I am not surprised that a small percentage of patients having chronic sinusitis, on whom intranasal operations are performed, develop acute otitis media or even mastoiditis. The wonder is that more do not.

THE METABOLIC CHANGES IN HEMATOPORPHYRINURIA NOT OF DRUG ORIGIN.

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HEMATOPORPHYRIN is simply hematin without the iron. It is found in the normal urine in faint traces (Garrod). This amount is increased, though not enough to color the urine, in various morbid conditions, such as measles and rheumatic fever. It has no clinical importance so far as we know in these minute amounts. When it occurs in sufficient amount to color the urine, causing hematoporphyrinuria, the act is significant and often ominous.

Hematoporphyrinuria is best known in connection with the use of sulphonal, trional, and tetronal. But besides these drug cases, the condition occurs as the result of various other toxemias.

T. K. Monroe¹ reports a case of periodical vomiting in a boy, aged seven years, occurring about every two months, and each attack lasting about a fortnight, accompanied with hematoporphyrinuria and acetonuria. The attacks continued for two years, and the patient finally died of the disease. He reports, also, the case of a woman, aged thirty-six years, who suffered from multiple neuritis and a pelvic exudate, accompanied with hematoporphyrinuria. She recovered in about seven weeks. Also a third case, that of a woman, aged twenty-six years, who suffered from hematoporphyrinuria after having become chilled while bathing at sea. In these cases there was no drug poisoning and no internal hemorrhage.

W. Langdon Brown and H. O. Williams² report the case of a married woman, aged twenty-two years, who had three attacks

¹ Quarterly Journal of Medicine, 1907-08, i, 49.

² Lancet, 1909, i, 1105.

of abdominal pain and vomiting with hematoporphyrinuria, lasting several weeks. In the last attack she had three epileptiform fits and became delirious and drowsy, but finally recovered. The authors collected other cases of hematoporphyrinuria, not due to drugs, but associated with gastro-enteric disturbance and apparently due to intestinal toxemia.

From the reported cases it would seem that hematoporphyrinuria, when not due to drug poisoning, is due, therefore, to some toxemia or to some internal hemorrhage.

The following case does not surely belong to any of these groups. It is reported because of the exceptional opportunities which were furnished me for making blood and metabolism studies in connection with the progress of the case, through the courtesy and helpfulness of Dr. T. C. Roper, of the New York Hospital Laboratory, and of Dr. T. W. Hastings and Dr. Warren, of the Cornell University Medical College Laboratory.

Summary. Male, aged sixty-seven years. Apoplectic seizure with temporary hemiplegia, short excited and long confusional mental state, lasting about three months. Development of marked hematoporphyrinuria, lasting for two months. Seven nitrogen examinations, showing increase of kreatinin and rest nitrogen; no signs of hemolysis, no drug intervention, no known intestinal toxemia. Hematoporphyrinuria is evidence of a metabolism disorder, and not a sign of a serious blood condition.

Mr. J. T. J., aged sixty-seven years, married, two children; occupation, president and financier. The patient has been a very strong, rugged, hard-working man, never taking a vacation. He has never drunk alcohol in any form, nor tea or coffee; he has not used tobacco nor any drugs. His food habits are said to have been particularly intemperate. He would eat all kinds of food, including meat, in very great amount. About twelve years ago he had some heart trouble, for which he was sent to Nauheim for two successive years. He was relieved by these trips. He had an attack of vertigo in January, 1909. He recovered from this and continued his work.

On February 23, 1909, while at work in his office, he became confused and was unable to talk connectedly. An hour or so later he could not talk at all, and on attempting to do so would burst out crying. On attempting to walk, he was found to be paralyzed on the right side. He was placed in bed and slept during the night. The next day he tried to get up and dress, but was unable to do so on account of his right hemiplegia. He tried to talk, but failed, and his efforts would end in explosive crying. He had also some difficulty in swallowing. He was just able to sign his name to a power of attorney.

He improved slightly in the next week, and then went into a

semicomatose state, which lasted for two days, during which period he would at times arouse himself and become delirious. He came out of this coma and was then more quiet, but was confused and at times delusional, thinking that he was being persecuted and poisoned. He could speak now a little, but his speech was very indistinct, and he could not sit up or stand without help.

He again gradually improved and in about a month after the beginning of the attack he was able to be brought to New York. At that time he could talk a little and could sit and stand, but the fatigue of the journey set him back; so that when he reached here he was again in a condition of semicoma, from which he would occasionally arouse and become delirious—trying to get out of bed and showing evidences of hallucinations of sight and hearing.

I saw him first on March 25, two days after he reached the city. He had then quieted down somewhat, and responded to simple questions and recognized members of his family.

On examination, he showed absolutely no signs of a hemiplegia. His right arm and leg were as strong as the left. There was no change in the reflexes, either superficial or deep. There was no Babinski reflex; no ankle clonus; no disturbance of deep or superficial sensation. His only peculiarity was a tendency to hold the left hand in whatever position it was placed—a sort of catatonic state. His special senses were apparently normal, though his mental condition prevented careful examination. The temperature was normal; the heart sounds good; the pulse 70; the blood pressure nearly 200 mm. Hg, and but a little higher on the left than on the right. He had for three days Cheyne-Stokes respiration; the lungs were normal. The urine showed a trace of albumin and some casts; the amount was normal.

During the next few weeks his condition slowly and regularly improved. He had attacks of explosive and involuntary crying when any one came into the room, or when a question was asked, or when he tried to talk much. For the first few days he was often delirious at night, and talked constantly of murder and plots against him, and at times refused medication, saying that he was being poisoned.

At the end of the third week he had quieted down and was free from any distinct irrationality or delusion. He was at that time still unable to talk freely or to speak anything but short sentences. He recognized his family, but did not know where he was. He could not write nor apparently read. He did not remember where he was during the past winter; did not know where he lived, nor where he was at that time; did not know where his children were. He remembered having seen his daughter on that day, but not his wife. He had no appreciation of values, and

did not know how much it was costing him to live, or how much could be done with a ten dollar bill. He could sign his name with difficulty. He could not read except isolated words. He could not name objects seen, heard, or felt. He formed correct sentences, but was unable to connect them or make continuous statements. In other words, he was completely disoriented and had amnesia of the past and to some extent of the present. He had a certain form of aphasia, which seemed to be a part of his general amnesia and clouded intelligence. In more technical words, he had apraxia (loss of power to do things because of loss of knowledge how to do them) and agnosia (loss of memory of the use of an object). He did not, for example, know how to use a knife or fork or spoon, and had to be fed, although he had no hemiplegia and he knew the name of the object.

He gradually improved, and in about two weeks was better along nearly all lines. His speech was more coherent, but he soon wandered off and became confused.

On April 29, five weeks after he reached New York, he had got so that he could recall the past fairly well and could tell about his past life. He talked coherently, his explosive sobbing ceased, and his delusions of persecution disappeared.

He gradually regained all his mental functions, so that by the last of May, three months after his illness began, he was able to read and write and converse. All signs of aphasia, agnosia, and apraxia disappeared; his mind was clear, and there was also nothing in his condition which would suggest that he was a sick man, except that his mind worked a little more slowly than usual and was a little more easily fatigued.

In November, 1909, he was seen by me again. He was then well and had no hematoporphyrin in the urine.

Details of Physical Examination. The *hematoporphyrinuria* was first noted about April 1, and it lasted till late in May.

The urine on admission, March 23, showed a specific gravity of 1022; it was of acid reaction, dark amber color; a faint trace of albumin, hyaline and granular casts, and a moderate number of red blood cells were present; indican was increased; there was no sugar; the daily amount was about 1200 c.c. (Dr. Roper).

On April 1, the urine was noted to be a reddish amber color.

On April 9 the reaction to hematoporphyrin was obtained. At this time there were no red blood cells found in the centrifuged specimen. There was still a faint trace of albumin and there were a few hyalogranular and hyaline casts; amount, 1000 c.c.; specific gravity, 1018.

On April 20 all drugs were stopped and he was placed on a meat-free diet for about one week, but the hematoporphyrin continued to be present. It very gradually decreased in amount,

yet when the patient was discharged nearly well in May, there was still some present. The trace of albumin became of the faintest, and at the last there were only a few hyaline casts.

At the time when the hematoporphyrin was first found the patient was rather excited, and at times at night delirious, and he thought that people were trying to poison him. This condition cleared up in about a week (April 19).

The blood pressure on admission was nearly 200 mm. Hg. On the second day it was 158, and after this it ranged about 160 to 150; finally, April 20 to 25, it was 140.

The pulse was at first about 90 (84 to 104). After about three weeks it dropped to 72 to 80, and when discharged it was about 70 (66 to 72) (May 3). The temperature was normal.

The respirations were about 20 (16 to 22) and on the first few days were at times of Cheyne-Stokes character.

The Blood Examinations by Dr. Roper. On admission, March 24: Hemoglobin, 90 per cent.; leukocytes, 12,800; polynuclears, 70 per cent.; small lymphocytes, 22 per cent.; large lymphocytes, 5 per cent.; eosinophiles, 2 per cent.; basophiles, 1 per cent. April 12: Hemoglobin, 96 per cent.; leukocytes, 8600; polynuclears, 76 per cent.; small lymphocytes, 19 per cent.; large lymphocytes, 2 per cent.; eosinophiles, 2.5 per cent.; basophiles, 0.5 per cent.

A Wassermann test for lues was made in November, 1909, by Dr. Hastings. It was negative.

Drugs. On admission the patient was given once 15 grains of trional; nitroglycerin, $\frac{1}{150}$ grain every two hours; and potassium iodide, 5 grains three times a day. On March 25 he was given sodium bromide, 15 grains three times a day for one day. On March 26 he was given a 5-grain blue mass pill and Rochelle salt, 1 ounce, and the potassium iodide was increased to 15 grains three times a day. On April 1 he was given 2 compressed cathartic pills. From April 1 to April 20 he received sodium bromide, about 30 grains daily; 2 grains of calomel once; dilute hydrochloric acid, 10 minims three times daily for three days; and a laxative pill—but no other medication, and no sulphonal or other hypnotic. On April 20 all drugs were stopped.

Food. The patient was fed on milk, eggs, bread, stewed fruit, and later, the ordinary hospital dietary of meat and vegetables. He ate normally and moderately. The stools were normal apparently. At one period all meat was excluded from the diet.

Nitrogen Examinations. The total urine under a fixed diet was examined by Dr. Roper five times, and by Drs. Hastings and Warren twice.

The appended table shows the results:

	Total N.	Urea N.	Ammonia N.	Uric or Purin acid N.	Kreatinin N.	Unde- termined N.
Hospital Diet, April 17 to 18, 1750 c.c.	10.1 ...	8.2 81.2	0.4 4.0	0.041 0.43	0.86 5.5	0.6 5.9
April 21 to 22, 1200 c.c.	5.56	76.0	6.0	2.4	3.4	12.2
Drug free diet, April 23 to 24, 1300 c.c.	8.4 ...	6.9 82.15	0.3 3.6	0.08 0.95	0.8 9.5	0.32 3.8
Meat-free diet, April 26 to 27, 750 c.c.	6.1 ...	5.1 83.6	0.27 4.4	0.09 1.5	0.49 5.0	0.15 2.5
Meat-free diet, April 28 to 29, 1100 c.c.	6.8	5.7	0.2	0.05	0.61	0.24
Meat-free diet, April 29 to 30, 1320 c.c.	8.1 ...	6.4 79.0	0.27 3.3	0.13 1.6	0.75 9.3	0.55 6.8
Meat-free diet, May 12 to 13, 1300 c.c.	9.82	83.7	5.2	2.4	5.8	2.9
Normal	10-14	85-90	3-5	0.0-1.5	3-4	2-6

The upper figures represent the actual amounts, the lower figures the percentage distribution of nitrogen.

Dr. Roper states: "All of these specimens were brownish in color, showed two bands corresponding in position to those of oxy-hemoglobin. These were not altered by the addition of glacial acetic acid or reducing agents. No reactions for blood pigment could be obtained. Acidifying with strong HCl changed bands to those of acid hematoporphyrin. Precipitation with BaCl and extraction with acid alcohol after washing with water and absolute alcohol gave a brilliant pink fluid, showing two banded spectrum of acid hematoporphyrin, which changed on making faintly alkaline to the four banded spectrum of alkaline hematoporphyrin. The urine also showed the absorption band of urobilin."

The clinical history would indicate that the patient suffered from an incomplete cerebral thrombosis, involving probably the left frontal lobe. This diagnosis was concurred in by Dr. Allen Starr, who saw the patient in consultation.

The psychosis which resulted was of the confusional and toxic type seen in persons at any age; but the temporary hemiplegia, the agnosia, and apraxia showed that there must have been more than a functional and toxic disturbance.

The study of the blood and urine show that the hematoporphyrin was not the result of a breaking up of blood cells, either living or

from a brain clot, for there would then have been some hematin or iron-bearing product. It leads to the conclusion that perhaps the hematoporphyrin in drug cases is due to metabolic (liver?) disorders, and not to a hemolysis, as has been usually supposed.

This view is supported by the fact that in hematoporphyrinuria due to drugs the liver cells show fatty degeneration.

The significance of hematoporphyrinuria apart from drug poisoning and perhaps from intestinal toxemia is not well known.

It has been demonstrated by Garrod and by Soberheim³ that hematoporphyrinuria may be present in urine after the dark color has disappeared and that, in other words, the color of the urine in this condition is not due to the hematoporphyrin, but to other abnormal pigments. It may, therefore, be that hematoporphyrinuria may be present in the urine without any change in the color. It may be inferred from the present case that its presence is not of so ominous significance as it seems to be in drug cases.

A METABOLIC STUDY OF MYOTONIA ATROPHICA.¹

WITH THE REPORT OF TWO CASES.

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THE case which forms the basis of the following considerations is interesting in several connections: (1) Because it represents a rare clinical entity; (2) because it showed in the light of metabolic study, some findings more marked than is customary in analogous conditions; (3) because one of the findings is now reported for the first time in connection with the disease; and (4) because such metabolic observations seem to throw light on the classification of the condition and suggest a means of arriving at a true diagnosis in obscure diseases of this nature.

A. B., aged thirty-seven years, white, female, married

Chief Complaint. Stiffness in the shoulder, elbow, and knee; pain in the back, and difficulty in walking

Family History. Negative, except that the patient is fairly confident that a sister who died in childbirth had an involvement of the hands similar to hers, but was otherwise healthy.

³ Deut. med. Woch., 1892, xviii, 566.

¹ Read at a meeting of the College of Physicians of Philadelphia, December 7, 1910.

Social History. She menstruated at the age of fourteen years, has been regular ever since, and was married at the age of twenty years. She has three children living, two of them healthy, and has had one miscarriage; one child died at birth with convulsions. A boy, aged about ten years, has hydrocephalus and is in a school for feeble-minded children. The patient states that he has some similar difficulty on opening his hands after tightly closing them, but this did not appear when he was examined. She does housework and formerly drank a small quantity of beer at intervals, but has had none for ten months; takes coffee and tea once daily.

Medical History. She has had measles and pertussis when a child, and diphtheria twelve years ago. She has never been ill in bed except for confinements and was well until the onset of the present trouble seven years ago.

Present Illness. Seven years ago she noticed a weakness in her knees which prevented her from going up stairs readily, although she otherwise felt well. With the aid of a little support she could manage easily and had no difficulty in walking on the level. The weakness in her legs became slightly more marked and one year later, after a childbirth, she developed a dull aching pain in the back. This pain has persisted on and off up to the present time. The weakness of her legs slowly increased so that four years ago she began to place her hands on her knees when she wanted to rise from a sitting posture. Three months ago she noticed some weakness in her left arm and shoulder which prevented her raising her arm over the back of her head and caused her to lean forward to comb her hair. This last development she thinks came on rather suddenly; she says she went to bed well one night and got up the next day weak, as described. She says that long before the onset of her attack she had difficulty in opening her hand after closing it tightly. When she presses her tongue against her front teeth, she cannot for a few seconds protrude it or talk. This condition she says is of recent development (a matter of a few months), though she does not know exactly how long. Her bowels have been a little loose, but she has had no difficulty in urination.

Physical Examination. This shows a rather adipose woman of large build, prominent forehead and good intelligence (Fig. 1). There is marked prominence of the seventh cervical vertebra posteriorly and the back, as a whole, is round. The tongue shows a slight moist fur and is easily and evenly protruded except as above described. The eyes give normal motions and reactions, except that the eyelids can be opened with ease against the resistance of the patient. Dentition is poor and teeth are poorly cared for.

The radial pulse is regular and of good volume, rate, and tension; the cardiac outline is normal and the sounds are good without murmur. The lungs are apparently normal. The liver extends from the fifth rib to the costal margin. The abdomen is large and relaxed, showing numerous striæ, but otherwise is negative.

Reflexes and Musculature. The eye-lids can be easily opened against the patient's resistance as mentioned, but the control of the muscles of expression is good, and there is no asymmetry of the face. No weakness of the temporals or masseter can be developed and the mouth can be drawn equally to either side, but when told to smile, the angles are not much retracted. The head is held markedly forward during the acts of sitting down or getting up. The neck is rather plump and there is a very slight swelling of the



FIG. 1.—Photograph of the patient, showing the suggestion of ptosis from weakness of the levatores palpebrarum.

thyroid which, according to the patient, has existed in its present state for years. The sternocleidomastoids cannot be clearly felt and turning the head in various positions does not make them conspicuous. The scapulæ are both prominent on the inner edges, especially the left scapula, which protrudes markedly when the left arm and shoulder are moved. There is some evident wasting of the associated muscles, especially visible on the inner side of the scapula, but adiposity masks its exact distribution. Anteriorly the chest seems flat in the upper part and the pectorals seem less developed than



FIG. 2



FIG. 3



FIG. 4



FIG. 5

FIGS. 2, 3, 4, and 5.—The pictures of the patient's hand show the successive positions assumed in the attempt to open it after forcible closure.

normally. There is no evident wasting in the deltoid, arm, or forearm region. The biceps and triceps reflexes are greatly diminished or absent. The patient has diminished but moderate strength in both arms (for acts not involving the shoulder girdle), but the shoulder muscles on the left are so weak that the left arm cannot be actively raised high enough to place her hand on her head. Passive movement of all limbs, however, is everywhere free. The hands are well formed and the fingers rather tapering. The power of contraction of both hands is below par and when closed as firmly as possible there occurs, for a few seconds, an inability to open the hands again (Figs. 2, 3, 4 and 5). When opening them, the fore and middle fingers are extended first, followed by the third and fourth in a slow athetoid manner, after which the thumb is extended and then finally the whole hand and palm are opened flat. Sometime the third and fourth fingers are opened first, but the general movement is always the same. There is also a tendency for the thumbs to be held adducted across the hands.

The power in each leg is everywhere below normal. The left is larger than the right and has been so, she says, since the birth of her last child when she had "milk leg." It is not oedematous. The right seems to be slightly less than normal in size below the knee, there is relatively little calf, for the general build of the limb, and the muscles of the calf seem rather soft and flabby on palpation. The thighs seem smaller than they should be and there is, possibly, some flattening of the vasti externi. The left leg below the knee is, perhaps, slightly firmer to palpation than the right, but the patient feels that the power in each is about equal. The buttocks seem to be less protuberant than in health, but the gluteal crease is equal on each side and adiposity masks the true condition of the muscles here. On rising from a sitting posture, the patient places her hands on her knees to obtain greater support. In getting up from the floor she rises on one knee, then gets on all fours, finally puts out one leg and by the support of a hand on a chair, for example, rises. She cannot get up without this external aid. In walking the alignment of the feet is rather poor, though not incoordinate. The patellar jerks are diminished, though present, and there is neither Babinski's sign nor ankle clonus.

Urine. Acid, with a granular sediment, a few white blood corpuscles, and some epithelium.

On October 27 the systolic blood pressure was 96 mm. Hg. and the diastolic 65.

On October 29 the eye fundus showed no change though there was beginning opacity of both lenses.

The leukocyte count was never higher than 8650 and the differential count was normal. Hemoglobin, 88 per cent.

The patient stated (April 28, 1910) that in swallowing she sometimes has some difficulty, which is of fairly recent development.

On April 28, 1910, the electrical reactions were tested by Dr. J. W. McConnell and found to show some diminution of response, about equal everywhere, but there was no indication of the reactions of degeneration.

Weight, on October 14, 1909, 153 pounds (69.54 kilos).

Weight, on October 22, 1909, 157 pounds.

The patient is a sufferer from psoriasis which is worse in summer. On August 23, 1910, about ten weeks since last previous examination and about ten months since she first presented herself, she said she felt that she was slowly growing worse and had recently developed some unsteadiness of station which she thought was not due to weakness. She complained of some slight difficulty in swallowing. On examination, her pupillary reactions were found as before and her station with the eyes shut was good. On rising, however, or on stopping suddenly when walking, she would, at times, show the above unsteadiness. She also complained of increasing difficulty in performing her work. The thenar and hypothenar showed some suggestion of atrophy though it was not marked.

Subsequently to the completion of the metabolic studies upon the present case, here to be reported, I had the opportunity to examine another instance of the same condition. It occurred at the Philadelphia General Hospital in the service of Dr. D. J. McCarthy who has very kindly given his permission to have it included in the present paper. For this courtesy, I wish to express his appreciation.

Social and Medical History. The patient is a white male, aged forty-two years, formerly married, but only for a few months, when he left his wife for infidelity. He had no children. His family history is negative for any analogous condition, though one brother now has phthisis and one sister cannot talk loud; possibly as the result of diphtheria and some operation connected with it. The patient's birth was normal, and he was the fifth member of the family. He says that he had repeated attacks of diarrhoea until two years of age, when he developed "St. Vitus' dance." At intervals of two years afterward, and until he was twenty-six years old, he had recurrent attacks of it, for which he took Fowler's solution, up to thirteen minims three times a day, which always relieved him. Otherwise, he says, he always felt well, except that at the age of sixteen years he had "bronchitis," which confined him to bed for a month. At one time he injured his eyes on a bet by looking at the sun for five minutes at 3 o'clock of a bright afternoon. This wager resulted in blindness, which lasted three weeks, since when he has worn glasses. He says that from fourteen to nineteen years of age he was subject to headaches, which were relieved for five years by the removal of a nasal polyp, but they then recurred, and he now has a slight frontal headache much of the time. His voice is somewhat nasal. He denies all venereal history.

Present Illness. The onset of his present trouble dates back seventeen years, when he was a nurse in a large hospital. A fall called his attention to the fact that his feet flopped in walking and that his legs seemed weak. His knees soon became affected, causing him to fall more frequently and his progress from that time has been steadily worse. Ten years ago he first developed some symptoms of Thomsen's disease, seven years after the weakness in his legs began, and now experiences frequently a "locking" of the limbs when he rises from sitting or begins almost any act involving the arms or legs.

Physical Examination. Examination shows a well-nourished and intelligent man of 5 ft. 7 in. He is "pot bellied" from accentuation of the dorso-lumbar curve. The facial expression is intelligent and tranquil. The extraocular movements are apparently normal though there may be some slight weakness of convergence. The pupils are equal and react well to accommodation, but sluggishly to light. There is some ptosis when the patient looks before him. The orbicularis and levator palpebrarum are markedly weak and there is twitching of fasciculi of the orbicularis palpebrarum on the left which, he says, has been present for seven years. There is slight weakness of the buccinators, but not of the orbicularis oris. The tongue is protruded evenly and easily in midline and is clean, without fissure, atrophy, or tremor. The sternocleidomastoids are greatly atrophied and when the head is put back it cannot be brought forward without great effort. There is free passive and active motion of both arms and coordination is good.

There is no atrophy of the subscapular group on either side, but both supraspinati show some atrophy, especially on the left. The left deltoid shows marked atrophy, but the right apparently shows none. There is slight atrophy of the biceps and triceps on the left, and a very little on the right. There is considerable loss of extensor power on the right. Flexor power of the right arm is good, of the left moderate. There is moderate atrophy of both forearms, especially of the ulnar flexor group, and the grip is reduced 50 per cent. Both thenar and hypothenar eminences show slight atrophy, and it is moderate in all the interossei. The triceps reflexes are present on both sides on reinforcement, but the biceps can be obtained only on the right.

The legs everywhere show wasting, though the right is slightly larger than the left. There is a corresponding and moderate loss of power in both legs. The knees are both hypotonic and the knee caps protrude anteriorly. The vasti externi share in the general wasting and probably suffer slightly, though not markedly, more than the rest of the leg muscles. The flexors of the foot show weakness. There is no knee jerk, ankle clonus, or Babinski sign, and there is no tenderness over the nerve trunks. The toes flex to plantar irritation.

The station with the eyes open or shut is good, though there is some instability because of weakness in the legs. There is a steppage gait. The hands show the myotonic feature of inability to relax for a few seconds after forcible closure and finally relax in a slow athetoid manner. The legs "lock," that is, become fixed in position when he starts to walk, as do the arms also for certain acts, and when the legs are affected his whole body remains apparently motionless for an instant. When the limbs are locked, the muscles concerned are contracted.

The intrathoracic and intra-abdominal organs present no important abnormalities, though both testes show atrophy, especially the left. The patient has no sexual desire and erections are involuntary. He cannot retain his urine as long as normally.

A review of the bibliography reveals the fact that but one report of this interesting condition has been made in American literature, so far as the author can ascertain,² although in all a total of twenty-five cases have been reported by foreign observers. In 1897, Pelizaeus called attention to a case evidencing the phenomenon of Thomsen's disease (myotonia congenita) with symptoms of muscular atrophy, and another instance was reported in 1899, by Nogues and Sirol. In 1900, Hoffman contributed a study which showed that muscular atrophy occurs in approximately 9 per cent. of cases of Thomsen's disease, since when there has appeared a number of articles recording the association of muscular atrophy with manifestations of Thomsen's disease and sometimes of myasthenia. Probably the most complete exposition is contained in a monograph by Batten and Gibb.³ Various names have been applied to this syndrome, the present nomenclature of which is redundant and confusing to the student. Rossolimo first used the term "myotonia atrophica" because it serves shortly to describe the salient features, but this bears an unfortunate resemblance in sound to myotonia congenita (Thomsen's disease), and to myatonia congenita or amyotonia congenita. Other terms employed have been "myotonia with muscular atrophy" (Lannois), "muscular atrophy with the electrical reactions of Thomsen's disease" (Lortat, Jacob and Thaon), "Thomsen's disease with muscular atrophy" (Nogues and Sirol), "Atypical forms of Thomsen's disease" (Pelz), "Muscular atrophy with slow relaxation of muscles" (Kleist), but myotonia atrophica is that most frequently applied. The term "myotonia" is objected to by some, since it is occasionally used as synonymous with Thomsen's disease and, similarly, the use of the adjective "atrophica" has found disfavor because the order of events is not always as the title suggests, that of dystrophy followed

² Hunt, Ramsay. Myotonia Atrophica, Jour. Nervous and Mental Diseases, 1908, xxxv, 269.

³ Brain, 1909, xxxii, 187.

by atrophy and also because the atrophy may not occur in the muscles affected. It is not the purpose of this article to consider at length, as has been well done elsewhere, the clinical features and variations of this disease, but the rarity of the condition demands, perhaps, a few words of exposition as to the leading characteristics.

There seems to be a familial tendency in regard to its occurrence, as might be expected in view of the hereditary nature of Thomsen's disease, but the etiology is at present quite obscure. The disease more commonly affects males between twenty and thirty, and the myotonic feature usually precedes the atrophy, though, as above indicated, this order is by no means constant. The sex of the first case here reported is interesting, since the few recorded cases leave no doubt that the disease is commoner among males. In only 3 out of 20 cases were the patients women, and in 2 of these the symptoms were so slight as to have escaped observation until it was attracted by the presence of the affection in a more marked degree in other members of the family. The condition begins insidiously, with or without a previous history of myotonic symptoms and with varying degrees of incapacity. When the case has developed, examination reveals muscular atrophy in the face, especially in the orbicularis palpebrarum and orbicularis oris, with occasional involvement of the mandibular group or the sternocleidomastoids. Of the upper extremities the forearm may be wasted, but the hand muscles are usually well preserved. The vasti of the thigh generally show atrophy, as do sometimes the peroneal and anterior tibial group, but elsewhere in the body the musculature escapes, except for a rare affection of the laryngeal. That the distribution of the atrophy may vary is well illustrated by the case of Steinert's that came to autopsy in which, contrary to the usual distribution, the hands and general musculature of the body were involved. According to Batten and Gibb, the muscles of the shoulder and upper arm are rarely affected, but in a few cases there has been noticed a wasting of the supraspinati and infraspinati. The myotonic symptoms are usually not widespread and are generally best or solely exhibited in the grasp of the hand. Flexion of the fingers and hand around an object is usually well performed, but on attempting to relax, a considerable interval must elapse before the hand can be straightened out; and even then this may be accomplished by a somewhat athetoid contortion. The greater the force of the grasp, the greater the difficulty of undoing it, though, after repeating the act a few times, it is finally easily accomplished. The difficulty of relaxation is not due to weakness of the extensors. The tongue may occasionally show involvement and there have been recorded instances in which this disability affected the upper arm and neck, but the legs are usually but slightly implicated. There are also instances in which perfectly typical cases of myotonia congenita have been affected with

muscular dystrophy (Steinert), but in these the myotonia preceded the atrophy, had existed from childhood, and was widely distributed. Collins⁴ has described a curious condition in which there were present extensive myotonic symptoms or purposive movements which affected the whole body and were accompanied by some hypertrophy. The myotonia, however, tended to increase as long as the movements were kept up and there was no atrophy, no myotonic reaction, or familial history. There also seemed to be some evidence of hysteria.

The electrical reactions in the disease under consideration, show a diminution of irritability to the faradic current, but nothing more. The pathology of the disease is confined to the study of one or two cases by Rossolimo and Steinert, the latter of whom has recently made a complete examination and has shown that the condition of the muscles is the same as in other myopathic cases. He found, however, degeneration of the posterior column in the lumbar region which could be traced up into the cervical, but he regards the cord condition as purely incidental. He agrees with Hoffman that these cases are true instances of Thomsen's disease and sums up his conclusions as follows: "The so-called 'myotonia atrophica' is a condition in which a typical case of Thomsen's disease is affected with muscular dystrophy. The clinical feature of this atrophy is sharply defined and highly characteristic. It occurs only in this form in Thomsen's disease. The comparative frequency of impotence and atrophy of the testicle should be emphasized." More recently a suggestive case in a female, aged thirty-four years, has been reported by Steinert in which the symptoms of the menopause had occurred. Sometimes the myotonic features are late in appearing and occasionally the myotonia has followed myopathy. Batten is inclined to place these cases in the great group of myopathies, but in his own words, further clinical and pathological experience is required before any definite statement can be made.

It will be seen from a consideration of the above that the present case can be best categorized by inclusion in the group designated myotonia atrophica, and I wish to express my obligation to Dr. William G. Spiller for helping me to a diagnosis and for emphasizing the neurological interest involved.

When the patient first presented herself at the dispensary for treatment, it seemed that observations on the general metabolism, creatinin, and calcium in particular, would be of interest and might help to classify the condition, especially in view of the results of some similar investigations conducted recently on a case of myasthenia gravis.⁵

⁴ Postgraduate, New York, 1905, xx, 516, 519.

⁵ Pemberton, A Study of the Metabolism of Myasthenic Gravis, with a Suggestion Regarding Treatment, AMER. JOUR. MED. SCI., 1910, cxix, 816.

In this last instance a rather low creatinin output was observed together with a very marked loss of calcium. A low creatinin output in myasthenia has been noted by Spriggs, though not so low as in the case referred to, but the calcium determinations just recorded were then made for the first time in this condition and were of considerable interest. The loss of calcium in seven days amounted to over 9 grams, and after the administration of this element for over two years by Dr. William G. Spiller, under whose care the patient was, recovery was practically complete and the patient now feels himself well. A consideration of this and of the other close relations which have been shown to exist between calcium and various muscular phenomena, emphasized the advisability of extending the observation to other muscular aberrations.

As far as I am aware no metabolic study of the calcium metabolism is on record in regard to either muscular dystrophy or Thomsen's disease, and the present case seemed a fitting one in which to attempt such a determination. Indeed, no attempt has been made to approach the question from any standpoint other than the clinical, beyond the suggestion made some years ago that veratrum poisoning in frogs caused somewhat similar phenomena on electrical stimulation, and that the condition might be referable to some metabolic disturbance. After a day or two of observation in the dispensary the patient was admitted October 7, 1910, for the purpose of diagnostic and metabolic study to the service of Dr. Joseph Sailer, at the Presbyterian Hospital, to whom appreciative acknowledgment is due for the privilege of undertaking and reporting the work upon her when in the ward.

She was placed upon a generous weighed diet, which was adapted to suit her particular demands, and analyses were made over a period of five days on the urinary nitrogen, creatinin, and calcium and the fecal nitrogen and calcium. The patient had been living under circumstances of rather poor hygiene, had been worried about herself, and had been expending much effort in the care of her home. When she was put at rest in bed in the hospital, the physical quiet and generally favorable conditions reduced the strain from which she had suffered and improved her spirits and stimulated her appetite. The results were that she gained two pounds in five days and showed a nitrogen retention of 28 grams. In this same period the calcium metabolism presented almost a balance showing a trifling loss of 0.5668 grams.

The creatinin output in the case now under consideration was found to average 0.40278 grams per diem which gives the creatinin nitrogen expressed in terms of total urinary nitrogen as 1.77 per cent.

In a series of cases of various perversions of muscular function, including dystrophy, Spriggs⁶ observed an output of creatinin ranging from 0.5 gram to 3 grams, but in none recorded was it so

⁶ Quarterly Journal of Medicine, 1907, i, 63.

low as 0.40278. In myasthenia gravis (my case⁷), the creatinin output was 0.39155. Sprigg's adult case of dystrophy gave a daily average of 0.53 grams which is, however, a creatinin percentage as above of 1.7.

It has been found useful to observers generally to express the daily creatinin elimination in milligrams of creatinin per kilo of body weight and this ratio is called the creatinin co-efficient. In health it varies from 7 to 11 milligrams of creatinin nitrogen. In Sprigg's series he found the lowest co-efficient in the dystrophy cases which gave 2.2 and 4 milligrams respectively. The former of these was in a boy of only fifteen and three-quarter years.

Levene and Kristellar⁸ have also observed very low creatinin co-efficients; and one adult, aged twenty-one years, in their series of five cases of muscular dystrophy gave a co-efficient of only 0.7, but observations were made over a period of two days only and such an extremely low result is very exceptional. The other adults in their series averaged 3.16. Similarly other observers have recorded low results in dystrophy and in a number of pathological conditions, and Myers has found a co-efficient of 2 in two very discrepant old women studied by him. This is a very low figure, however, for adults, and the case now being reported is noteworthy in that the creatinin co-efficient was 2.0139.

This was not suggested, *a priori*, by the condition or the general activity of the patient, who is able to care for her own home and a family of five. While there was plainly atrophy of tissue in the scapular region, it did not seem excessive, and was further masked by the general adiposity. There was no pseudohypertrophy. A consideration of these results was an aid in classifying the disease from which the patient suffered and indicated more strongly than could clinical observations alone, its probable nature as well as the degree of involvement. It was possible to eliminate myasthenia gravis with relative ease, although in the past myotonia atrophica has been so diagnosed; but had there been more doubt as to this, a consideration of the calcium balance would have thrown weight in the same direction. This last needs corroboration by studies of other cases, but it is cited to indicate the use to which could be put the slowly increasing number of metabolic observations in these states, and the importance of studying such doubtful affections from a dynamic point of view.

More complete observations on the creatinin and calcium metabolism in dystrophy and several muscular perversions of function are now being made.

CONCLUSIONS. As far as the study of one case can be relied upon it may be said that there is apparently no significant disturbance of the calcium output in muscular dystrophy; at least, in the presence of those phenomena which suggest Thomsen's

⁷ AMER. JOUR. MED. SCI., 1910, cxi, 256.

⁸ Amer. Jour. Phys., xxiv, 45.

disease. This can probably be also inferred, though not surely, in regard to Thomsen's disease "per se." The creatinin output, however, under these circumstances may be considerably reduced and the creatinin co-efficient conspicuously low. A consideration of the calcium, creatinin, and general nitrogenous metabolism as recorded here, and in myasthenia gravis, may lead to information of value in classifying doubtful conditions of this nature and localizing the perversions of function. It seems that such investigations should be more frequently undertaken in careful clinical studies.

Finally, I desire to express, with appreciation, my indebtedness to Dr. James E. Talley for many courtesies shown me in the wards of the Presbyterian Hospital.

DIET.

	Eggs.	Bread	Milk	Rice.	Butter.
Oct. 13					
B	88	62	12		
D	84	70	12	65.1	55
S	85	51	12		
Oct. 14					
B	89	90	12		
D	91	70	12	57.2	99
S	89	65	12		
Oct. 15					
B	89.75	72	12		
D	85	80	12	63.90	32
S	89.50	67	12		
Oct. 16					
B	72	79	12		
D	96	72	12	69.70	89
S	84	76	12		
Oct. 17					
B	112	78.5	12		
D	97.50	80	12	51.60	60
S	109	27.5	12		
Total . .	1350.75	1040.0	180	307.50	335

PERCENTAGE CONTENTS OF FOODSTUFFS IN CA AND N.

	Per cent. calcium oxide.	Per cent. nitrogen.
Eggs	0.122	2.008
Bread	0.041	1.265
Milk	0.184	0.574 (1031 sp. gr.)
Rice	0.0145	1.110
Butter	0.030	0.080

TOTAL FOOD INGESTED.

		Grams.
Eggs.	Calcium	1.1771
	Nitrogen	27.1231
Bread	Calcium	0.3045
	Nitrogen	13.1560
Milk	Calcium	7.8049
	Nitrogen	34.0873
Rice	Calcium	0.0445
	Nitrogen	3.4143
Butter	Calcium	0.1073
	Nitrogen	0.2680

URINARY FIGURES FOR EACH DAY.

Oct. 14	590 c.c.	Grams,
	Creatinin	0.300
	Ca	0.1257
	N	6.720
Oct. 15	800 c.c.	
	Creatinin	0.386
	Ca	1907
	N	8.6240
Oct. 16	410 c.c.	
	Creatinin	0.2695
	Ca	0.1508
	N	4.6592
Oct. 17	1100 c.c.	
	Creatinin	0.5742
	Ca	0.2392
	N	12.0102
Oct. 18	1075 c.c.	
	Creatinin	0.4842
	Ca	0.2608
	N	10.2256

URINARY TOTALS.

Creatinin	2.0139
Calcium.	0.9672
Nitrogen	42.2390
Ca in total feces	9.0047
N in total feces	7.5413
Total ingested calcium	9.4041
Total excreted calcium	9.9719
Negative calcium balance.	0.5668
Total ingested nitrogen	78.0476
Total excreted nitrogen	49.7821
Positive nitrogen balance	28.2655
Daily average of creatinin excreted	0.40278
Total creatinin excreted	2.0139

Creatinin co-efficient = milligrams of creatinin (daily) nitrogen per
kilo of body weight = (normally) 7 to 11 milligrams.

Present ratio	0.149713	0.002138
	69.54	

The creatinin co-efficient in the present case is, therefore, 2.138 milligrams. The figures for the creatinin co-efficient are made up on the lowest body weight; they would be even less if made up on the average body weight or on the greatest body weight attained during the experiment. The percentage contents of the foodstuffs in Ca and N was taken from "A Study of the Metabolism of Acromegaly."⁹

⁹ Edsall and Miller, Univ. Penna. Med. Bull., xvi, 143.

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CHRONIC INFLUENZA AND ITS RELATION TO NEUROPATHY.

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My thesis is that influenza may be and frequently is a chronic intoxication.

The specificity of influenza was discovered in 1902, by Pfeiffer, more than four hundred years after epidemics of the disease were first accurately described. Most authorities state that the rate of mortality is very low, and the disease has presented little of general interest aside from its pandemicity, vagaries of onset and manifestations, and its multiplicity of complications. The mode of invasion is conceded to be through the respiratory tract, and the organism is usually found in the bronchial and nasal secretions. The bacillus often persists in secretions after subsidence of symptoms in severe cases. I have been much impressed with the belief that influenza might be a chronic, as well as acute infection, or, at least, a chronic intoxication, and my beliefs, while not proved by extensive clinical experience and data, have, at least, been partially corroborated by the general history of many cases of "grippe," reported by reliable investigators. In explanation of the frequent occurrence of *Bacillus influenzae* in the secretions of persons in normal health, or suffering from some other disease, such as tuberculosis, scarlet fever, measles, etc., attention may be called to the analogous occurrence of the causative organism of enteric fever, diphtheria, and cholera in persons not suffering from these diseases.

In order to throw more light on the cause and dissemination of epidemic influenza, B. Scheller made examinations of a large number of persons suffering from epidemic influenza, as well as apparently normal persons in Königsberg during the winters of 1906-07, 1907-08, 1908-09, and the summer of 1908. Swabs from the throats of cases diagnosticated clinically as influenza, cases of pulmonary tuberculosis, and normal individuals were examined, microscopically and culturally, for *Bacillus influenzae*. During an epidemic of influenza in the winter of 1906-07, 80 per cent. of the 56 cases of influenza showed the presence of *Bacillus influenzae* in pure culture in more than one-half the cases; 8 cases wrongly diagnosticated as tuberculosis, and 4 of pneumonia showed pure cultures of *Bacillus influenzae*. Of 109 normal persons examined, 25 (24 per cent.) were found to be "carriers" of *Bacillus influenzae*, 15 of these giving a history of at least one previous attack of the disease.

Osler, in his monograph on influenza, concludes that "since the late severe epidemics it has been the fashion to date various ailments or chronic ill-health from the disease." In many cases the deduction is certainly correct. It is astonishing to note the number of patients who have been crippled in health for years after an attack.

Chronic influenza in many respects certainly bears a close similarity to tuberculosis, and I have no doubt that many cases of chronic capillary bronchitis, pneumonia, bronchiectasis, etc., in which the disturbing factor was *Bacillus influenzae*, have been diagnosticated tuberculosis. This has, in a way, been confirmed by my study of three cases, which clinically presented symptoms and physical signs of tuberculosis, but in which the tubercle bacillus could not be isolated.

At autopsy the following results were found:

CASE I.—Pericarditis with serous effusion; bronchiectasis.

CASE II.—Carnification of the tip of the right lower lobe of the lung; hepatic enlargement, non-caseating nodules; complete fibrosis of the ovaries; and intramural fibrosis of the uterus.

CASE III.—Capillary bronchitis; atheroma of the aorta; sclerotic endocarditis; fibrosis of the ovaries, and catarrhal enterocolitis.

I admit that the pathological findings in these cases are as insufficient and indefinite as the clinical diagnosis of tuberculosis was justifiable, although the organism was not found. The pathological results were such as we should expect in the cases which have been selected from clinical reports in the vast amount of literature. Attention is especially directed to the last two cases which presented a diffuse fibroid degeneration of the ovaries. This was certainly non-tuberculous. *Could it result from chronic influenza?* Authorities have always emphasized the distressing effects of "la grippe" on the female genitalia. No disease is more to be dreaded as an

intercurrent affection during pregnancy or the puerperium, because of the frequency of abortion and the occurrence of menstrual irregularities.

F. T. Lord, the pioneer in the study of influenza as a chronic disease, has written an extensive paper on the pathological and clinical similarity and confusion of influenza with tuberculosis, during epidemic and interepidemic periods. Jacobson, by injecting influenza bacilli with streptococci, and Slatineano, by injecting them with lactic acid into laboratory animals, claim to have obtained virulent cultures, capable of killing animals. "It is possible in patients with *Bacillus influenzae* in the sputa to get clumping of the bacilli suspended in normal saline solution (one-tenth or one-twentieth) of their blood serum." The results are inconstant.

Cantani also claims positive results, but his work has not been confirmed. The pathogenicity of *Bacillus influenzae* has been substantiated by exhaustive bacteriological and biochemical studies. Although the results of animal inoculation are unsatisfactory, "the impression is irresistible that the influenza bacillus is pathogenic for man when, in sputum preparations or stained sections from the lungs of patients who have died of bronchopneumonia the bacilli are found in enormous numbers, both within and without the cells, to the practical exclusion of other organisms." Within the last few years the organism has been found as the apparent sole infecting agent in several extrapulmonary regions. Heroosky obtained pure cultures of *Bacillus influenzae* from the pus of acute suppurative cholecystitis. Albrecht and Ghon found influenza bacilli as the only organism from a phlegmonous inflammation of the arm. Meunier, Nauwerk, and many others, report that the bacillus appeared to be the sole apparent cause of meningitis.

In man, therefore, the influenza bacillus must be regarded as capable of producing pathogenic processes without the aid of other organisms. The influenza bacillus must be regarded as the most important cause of a large number of cases of respiratory infection (acute and chronic) during the interepidemic periods; and as a contributing cause in many other cases when found mixed with the pneumococcus, *Micrococcus catarrhalis*, and other organisms.

Patients may carry the organism in enormous numbers for years in their sputum, just as they have been shown to carry other common representatives of the flora of the respiratory tract. The frontal, ethmoid, and maxillary sinuses are frequently infected and act as the nidus of infection in chronic cases. Many physicians have observed cases of intermittent fever occurring periodically in which the diagnosis has been well-nigh impossible, even when assisted by chemical and bacteriological tests. Could these cases be acute exacerbations of a chronic infection or intoxication by *Bacillus influenzae*?

Cerebrospinal meningitis while usually acute, may be intermittent or chronic, and *Diplococcus intracellularis meningitidis* can be isolated in pure culture by spinal puncture. *Bacillus influenzae* has always shown a predilection for the nervous system. Numerous cases of meningitis have been reported, but it was not until a few years ago that the organism was isolated from the spinal fluid in influenzal meningitis. Certainly, if the organism can produce and be isolated from the exudate of spinal meningeal inflammation, we must presume a diffused hemotogenous dissemination. The diplococcus of Weichselbaum, producing acute or chronic meningitis, protects from recurrence. Influenzal infections do not protect, but rather predispose to recurrences. This, together with the clinical history of prolonged indisposition, with exacerbations at irregular intervals, is axiomatic evidence of chronicity.

CASE I.—Mrs. P., female, white, aged sixty-two years, born in Virginia, has lived in Washington for the last fifty years. She gives history of no illness influencing the object of this report. She has had frequent colds in winter of each year for the last fifteen, before which time she was unusually hardy. In 1894 and 1895 she suffered from intermittent earache for several months; attacks being accompanied by headache and fever. The ear finally began discharging pus, and after a few weeks' treatment the discharge ceased, but the patient has since been quite deaf in the affected ear.

She came to me in December, 1907, suffering from what I presumed to be influenza, presenting the following symptoms: severe headache, lumbar pains, chills, fever, and cough, with mucopurulent expectoration. I gave the usual treatment for "grippe," to which she responded promptly. On the second day after leaving her bed she washed clothes all day, and on the following day I was again called.

The patient presented the same symptoms as before, but the cough was much more distressing and the expectoration profuse, fetid, and greenish yellow. The sputum examined for *Bacillus tuberculosis* was found negative. Urinalysis showed a slight trace of albumin.

Physical examination of chest showed numerous small, moist rales all over the chest, especially at the base, and bronchial fremitus. The breath sounds were harsh and arrhythmic at the base. The leukocyte count was 8300.

After remaining in bed several days under treatment, she was somewhat improved, but complained of great weakness, mental hebetude, indefinite neuralgic pains, and she looked apathetic. For two weeks she improved slowly, when, being exposed to damp, cold weather, she had a return of the cough and other symptoms. At this time, she showed the effects of these repeated attacks. She was anemic, had lost fifteen pounds in four weeks, was weak, and greatly depressed mentally. She continually expressed a willingness and desire to die, and her mental condition became distressing

to her relatives. Another examination of the sputum for *Bacillus tuberculosis* was made. At this time I felt firmly convinced that my patient was suffering from pulmonary tuberculosis, but tubercle bacilli could not be demonstrated in the sputum after exhaustive examinations. I then examined smears of the nasal and bronchial secretions for *Bacillus influenzae* and discovered an organism conforming in morphological and staining reactions to this organism. I then made glycerin-agar and ox-blood agar smear plates from the bronchial and nasal secretions, and found in mixed culture *Bacillus influenzae*. The cough has persisted with more or less severity for the last year and a half, and patient has had at least ten attacks of influenza. Examinations of the sputum made on three occasions in the last four months, show a continuation of the bacillus.

CASE II.—S. F., a female, white, aged sixty-four years, has had two attacks, the second of the gastro-intestinal type. The organism was present in the nasal and bronchial discharges for three months after the last attack. She steadily lost weight; and since her last illness has had at irregular intervals attacks of pain in the right upper quadrant of the abdomen, resembling gallstone colic. There is no history of hepatic or gall-bladder infection prior to the "grippe" infection.

CASE III.—J. McB., male, white, aged fifty-eight years. In February, 1908, the patient was attended by me during a typical attack of influenza. No examination for the bacillus was made, but a localized epidemic prevailed in Washington at the time. The patient apparently made a prompt recovery from the acute symptoms, although tardy in regaining his strength and normal tone. In June of 1908, while attending the wife of the patient, he complained to me of loss in weight, apathy, and nervous instability; he said he "had chills at irregular intervals, followed by fever and drenching sweats." He suffered from dyspnoea on exertion, and had noticed for the past three months that his ankles became swollen toward evening. He appeared to have lost considerable weight, was anemic, and, in comparison to his robust appearance before his attack in February, was physically a derelict. Examination for *Plasmodium malarie* was negative. Physical examination revealed marked increase in the area of cardiac dulness, with signs of mitral insufficiency and aortic stenosis.

He was put to bed and I called Dr. Thos. A. Claytor in consultation, who concurred in the findings as to heart, and in addition discovered the spleen markedly hypertrophied. The patient improved sufficiently to travel to Massachusetts, where he died several weeks after admission to a sanitarium.

The following cases excerpted from the literature are presented as bearing on influenza as a chronic infection.

F. C. Doble¹ reports a case of pericarditis and endocarditis

¹ *Lancet*, April, 1908.

appearing three days after very mild symptoms of influenza. The patient had a similar attack one year previous, and the physician (not Dr. Doble) told the patient he had "influenza of the heart." Doble says: "It is curious that the pericardium should be affected by so mild an attack of influenza, especially with slight bronchial symptoms. It seems to prove that *Bacillus influenzae* circulates in the blood early in the disease in even a mild form and produces a true septicemia."

R. D. Brown² discusses at length the relative increase in psychoses during influenza. He says: "That cases of mental disease are increased by influenza cannot be disputed. It is well recognized that very frequently a certain amount of lassitude, neurasthenia, or mental depression is present long after an attack of influenza, though of mild character and short duration." A patient once with influenza during the fall or winter means a patient until spring or summer. It has been suggested that it is the postinfluenzal exhaustion that is the important factor, but although this may be true in some cases, it is not in all. The mental symptoms appear very often as soon as the second or third day of the disease. The influenza bacillus or its toxin seems to be the exciting agent rather than the fever of postfebrile exhaustion. A peculiar feature is the liability of postinfluenzal psychoses to relapse.

Clouston, in 1890, said: "The microbe or the poison of influenza destroyed the cortical energy to a much larger extent than any of the continued fevers or zymotics; nay, its effects on the mental condition of Europe, during the years of its prevalence, far exceeded in destructive powers all those diseases put together. . . . It left the mental and nervous tone of Europe lower by some degrees than it found it."

Bezly Thorne, in 1890, looked upon influenza as a cerebrospinal malady, and at that time this view was generally accepted. In nearly every case he had found some portion of the spine tender three or four hours after the onset of the attack. Gilbert Smith, at the same time, believed the morbid agent, howsoever originally produced, might be further developed in the human body and become the source of increased contagion. C. E. Abbot reports a case of "double attack," the first occurring January 18, 1890, and followed by rapid convalescence, the second on April 3, 1890.

Sansom has been one of the best investigators of influenza. He reports a case in a man, aged fifty-three years, with "recurrent attacks of hepatalgia without jaundice and protracted enfeeblement for twenty months after the acute attack contracted in Paris. He classifies his cases of prolonged pain as follows:

² Scottish Med. Jour., 1902.

	Cases.
I. Epigastrium	9
Abdomen generally	2
Hepatic area localized	1
II. Head—various sites	7
Supra-orbital	1
Right inferior maxilla	1
III. Cardiac region	7
IV. Extremities—hips and legs	2
Calves	2
Arms	2
Right sciatic region.	1
Fingers	1
Lumbar region	1

In all of these cases the symptoms of pain and protracted enfeeblement were almost constant from six months to as many years after the acute attack, and some patients had recurrence of general symptoms of influenza at intervals.

F. T. Lord³ reports 11 chronic cases of influenza; "1 recovered, 1 died of cerebral hemorrhage, and 1 of chronic bronchiectasis and emphysema; 8 continued to cough with persistence of influenza bacilli in the sputa. "It is of interest to note that 5 of these patients were treated in the fall of 1902 at institutions for the cure of tuberculosis" (Lord).

The following cases, reported by F. T. Lord, are of great interest. Of 11 chronic cases, 2 died; 1 showed *Bacillus influenzae* for a period of four years, during which time she had chronic cough. The autopsy revealed diffuse bronchiectasis and emphysema. A second patient had an asthmatic cough for nineteen months before admission and the organism persisted in the sputum for one month. He died two years after the attack. No autopsy was made. "Of the 9 cases followed one to three years, 8 showed no material improvement since they first came under observation." Their cough improves somewhat each summer, to return with equal intensity in the winter.

Between August, 1902, and January, 1904, Lord examined the sputum from cases coming to the out-patient department of the Massachusetts General Hospital. Cases were unselected, except to exclude from investigation those patients in whom *Bacillus tuberculosis* was found. Clinically they suffered from acute or chronic disease of the respiratory tract. In 110 (59 per cent.) of the 186 cases an organism having the morphology and staining reaction of *Bacillus influenzae* was seen in varying numbers. In 56 cases (30 per cent. of all investigated) the organism was shown by culture to conform in all respects to the bacillus described by Pfeiffer in 1892, and regarded by him as the cause of epidemic influenza. In 47 cases (25 per cent. of all studied) the influenza bacilli were in overwhelming numbers. As the technique improved

³ Boston Med. and Surg. Jour., April, 1905.

the organism was found in somewhat larger proportions. The cases showing the bacilli in the sputum were quite evenly distributed over the eighteen months during which the investigations were pursued. No epidemic of acute influenza occurred during this period.

Chronic influenza as a contributing or as the sole cause of nervous disease is a subject which has been of interest to me. The merits of the assumption I shall be compelled to depend upon superior authority to prove or disprove. It is without question that organic and inorganic nerve disease results from acute influenza. Whether influenza is the original cause of psychoses acting as a chronic infection, or whether it is the contributing cause to a psychopathic basis, is a question which is beyond my knowledge of psychiatry. The history of influenzal epidemics has shown statistically that the mental and nerve force is lowered for a considerable time after the disappearance of the disease epidemically. A brief resume of a few of the symptoms and sequels, show a predominance of nervous involvement.

Prostration is frequent and far outlasts the symptoms of the disease. Vertigo, insomnia, delirium, and coma are not uncommon. Neuralgic pain is one of the most common disturbances, accompanying, persisting, and recurring irregularly, after the decline of fever and the subsidence of other symptoms. Myalgia, joint pains, hyperesthesia, anesthesia, neuritis may accompany and not infrequently follow attacks for lesser or greater periods. Neurasthenia, or more frequently cerebraesthesia, may be initiated, and the opinion is held that these neuroses are the result of chronic infections by influenza acting directly or through the medium of symptoms of localized inflammation. Epilepsy has immediately followed influenza. To conclude, I have submitted evidence which is far from adequate, but a theory that is strongly in favor of influenza as a chronic as well as an acute disease.

I am of the opinion that influenza is not only with us always as a chronic infection, but it is the source of acute cases occurring sporadically and endemically.

While I have not touched on the invasion of the accessory sinuses by the organism, in closing some consideration should be given this most frequent complication, or rather extension, of the local inflammation. *Bacillus influenzae* is responsible for a very large majority of cases of sinusitis, otitis, salpingitis, mastoiditis, and their sequels. The organism has been recovered in the discharge of more than 50 per cent. of patients suffering from suppurative otitis media, usually mixed with the pyogenic organisms. Dench claims that most all cases of maxillary sinusitis are the result of influenzal infection, and emphasizes the fact that the organism finally produces a low grade of inflammation with the formation of polyps and hypertrophy.

REVIEWS.

A SYSTEM OF MEDICINE. By Many Writers. Edited by SIR CLIFFORD ALLBUTT, K.C.B., Regius Professor of Physic in the University of Cambridge; and HUMPHRY DAVY ROLLESTON, M.D., Senior Physician to St. George's Hospital, London. Vol. VI; pp. 861. London: Macmillan & Co., 1909.

VOLUME VI of Allbutt and Rolleston's *System of Medicine* is devoted to diseases of the heart and bloodvessels—a convenient and appropriate arrangement. The volume opens with a brief though interesting chapter on the physics of the circulation, by James Mackenzie; this comprises a revision and amplification of Professor Sherrington's original introductory chapter on cardiac physics—added to, however, by some discussion of the peripheral circulation and blood pressure. Diseases of the pericardium are described very satisfactorily by Frederick T. Roberts, and the clinical descriptions are enhanced by several effective illustrations. Sir R. Douglas Powell discusses diseases of the myocardium and angina pectoris. It is, of course, difficult to separate diseases of the myocardium from other disorders of the heart, and the effort to do this is perhaps responsible for what seems to be a fragmentary and somewhat disconnected discussion. Amends, however, are made in the article on angina pectoris; although, here also one can scarcely escape the conviction that a little too much is made of angina pectoris vasomotoria. What is described as angina pectoris gravior is divided into secondary cardiac angina and primary cardiac angina—both well and ably discussed—albeit one may not be able always to make a differential diagnosis during life. Attention is directed to the fact that all too generally the outlook is deemed exceedingly grave, whereas, by resort to appropriate treatment, much may be done, not only to relieve symptoms, but to remedy the conditions which underlie them.

The volume owes much of its value to the two regius professors of physic who adorn the English profession. Professor Allbutt himself contributes articles on overstress of the heart, disease of the aortic area, and functional disorders. As is well known, he has devoted much time and patient thought to the study and investigation of the effect of mechanical strain on the heart and bloodvessels, and he has repeatedly given to the profession the results of his time and

efforts in language that well may excite the envy of others less well endowed. It were trite, therefore, to say that these articles must be read by all who would keep informed of what the master mind believes; but upon an occasion such as this one may venture to emphasize it. The discussion of fatigue, acute and chronic strain, and cognate subjects is as illuminating as it is convincing, and withal moderate in tone and cheerful in general outlook. The chapter on aortic valve diseases is replete with splendid clinical descriptions and wise counsels; his discussion of the relation of infections, mechanical strain, and the atheroma of senescence fulfils all the requirements of those who would become informed of the etiological factors; and his therapeutic recommendations reveal the close and experienced observer. He who has not yet become convinced of the value of morphine in many cases of advanced heart disease should read and ponder well what he says. Professor Osler, the other regius professor, in association with A. Keith, contributes a new article on Stokes-Adams disease, which comprises all known on the subject to date, as well as remarks on conditions of a related nature that necessarily enter into the differential diagnosis. He contributes also a new article on aneurysm—in his usual inimitable style.

There are some other notable contributions. G. A. Gibson has revised and enlarged the late A. E. Sansom's chapter on disease of the mitral valve, making it an even more valuable discussion than it was. Thomas McCrae has revised the late J. Dreschfeld's account of acute simple endocarditis. G. Newton Pitt describes diseases of the right side of the heart; I. Humphry, congenital diseases; and T. Oliver, injuries produced by electrical currents of high pressure. F. W. Mott has materially revised and somewhat amplified his chapter on arterial degenerations and diseases. M. H. Clutton describes phlebitis. The book closes with a revision by the junior editor, Dr. Rolleston, of Professor Welch's well-known articles on thrombosis and embolism, and a new article by himself on diseases of the lymphatic vessels.

All in all the volume is assuredly one of the most important of the series; and being devoted to the very absorbing and important subject of diseases of the heart and bloodvessels merits the attention of all practising physicians.

A. K.

A MANUAL OF OPERATIVE SURGERY. By SIR FREDERICK TREVES, BART., G.C.V.O., C.B., LL.D., F.R.C.S., and JONATHAN HUTCHINSON, F.R.C.S., Surgeon to the London Hospital. Third edition; in two volumes. Vol. II; pp. 821; 301 illustrations. Philadelphia and New York: Lea & Febiger, 1910.

THE first volume of this edition of Treves' *Operative Surgery* was reviewed in the November, 1910, number of this journal (page

742). The present volume completes the work, and deals with the head, neck, and spine, the thorax and breast, the vessels and nerves, amputations, the bones, joints, and tendons, the muscles, ligaments, and fasciæ.

The articles on the skull and brain, and on the middle ear and the mastoid antrum, have been revised and largely rewritten by Mr. A. J. Walton. The general teachings as to head injuries and brain diseases are in the main sound. In the section on the operative treatment of intracranial hemorrhage some confusion results from a certain indefiniteness in writing of extradural and subdural hemorrhages. Sir J. Hutchinson is quoted as having said, in 1867, that the modern annals of surgery do not contain any cases in which life has been saved by trephining for "this state of things." As both the preceding and the following paragraphs deal with the two forms of hemorrhage, it requires careful reading to determine which "state of things" is meant. Moreover, the remark has now only historical interest; and this is true of Preseott Hewett's statistics (1883) as to the frequency of injury to the middle meningeal artery. Much later, more extensive, and equally reliable figures are easily obtainable.

In the discussion of the surgical treatment of epilepsy no mention is made of the interesting fact that most epileptics are temporarily benefited by *any* operation, even if it has no relation to the condition. This fact obviously affects all statistics—among them some quoted by the author—as to operative results, unless a considerable period of time has elapsed before the cases are reported. In the article on cleft palate, the author's views as to the undesirability of very early operation are rather suggested—by quotations from Sir Thomas Smith—than expressed, and might well be emphasized.

There are certainly some advantages in many cases of cervical tuberculous adenitis in early ligation of the internal jugular, and also in the application of carbolic acid to certain sinuses and curetted gland cavities that may unavoidably be left. We cannot agree that the former is a "gratuitous complication" or the latter a "risky procedure that can do no good."

In the section on cancer of the breast exception is very properly taken to the statistics of operators who arbitrarily fix a time limit of three years or so as establishing a "cure."

In the article on interseapulothoracic amputation no mention is made of the suggestion of Le Conte, made in 1897, and repeated at the International Congress in Paris in 1900, that instead of the routine resection of the middle third of the clavicle, the inner end of that bone be disarticulated and the bone elevated, or—if it is necessary—removed prior to the ligation of the vessels. This has been adopted (without credit to Le Conte) by Berger.

Matas' aneurysmorrhaphy is described by quoting a paragraph

from the original article (1903) and dismissed with a brief comment, to the effect that the authors cannot see "that anything is gained by the procedure." No statistics are given. The many reported successes are not alluded to. In the section on amputation of the leg no mention whatever is made of the method of Matas, now widely used in this country, while the practically obsolete "Teale" method occupies a page and a half.

The same tendency to disproportionate reference to British surgery—as compared with that of other nations—is noticeable in this as in the previous volume. Numerically it is again as hundreds to dozens. This is a grave defect that should not be perpetuated in subsequent editions. Nevertheless, the work as a whole is of distinct usefulness to the operating surgeon, though a catholic revision would have made it far more so. The new colored plates are excellent, and the illustrations are uniformly clear and instructive. The book is beautifully made.

J. W. W.

HOOKEWORM DISEASE: ITS ETIOLOGY, PATHOLOGY, DIAGNOSIS, PROGNOSIS, PROPHYLAXIS, AND TREATMENT. By GEORGE DOCK, A.M., M.D., Professor of the Theory and Practice of Medicine in Tulane University, New Orleans; and CHARLES C. BASS, M.D., Instructor in Clinical Microscopy and Clinical Medicine in Tulane University, New Orleans. Pp. 250; 49 illustrations. St. Louis: C. V. Mosby, 1910.

UNLIKE many monographs which, on account of the rapidly progressing knowledge upon the subject, are valuable today, inasmuch as they reflect a passing view, but are out of date tomorrow, by reason of added information, this book of 250 pages gives a complete and nearly finished presentation of the important disease caused by *Ankylostoma duodenale*. The facts concerning all aspects of the disease processes, etiology, and treatment are for the most part well known, and except for certain details, perhaps it is possible to present the subject in complete and comparatively lasting form. This the authors have done in an admirable manner. It is scarcely necessary to mention the importance of this disease, not alone from the medical standpoint, but on account of the great economic and industrial problem which it entails. It is, therefore, highly desirable that, aside from the numerous articles, a readily accessible book containing all the necessary information upon the subject should be available. This book is therefore of great value. It is written so clearly that it affords a source of information for anyone who has the least interest in the matter, and is so fully illustrated that it affords an excellent guide to the practical study of the question. Though most of the cuts are excellently chosen,

it is to be hoped that in another edition a good original drawing of ovarian stages of the development of the egg and embryo of the hookworm will be substituted for the poor cut taken from Perroneito. We cannot help feeling, too, that the book would have been more valuable if many of the important references, at least, had been given. This, however, does not really impair its usefulness as a book presenting complete information concerning Hookworm Disease.

W. T. L.

A PRACTICAL STUDY OF MALARIA. By WILLIAM H. DEADERICK, M.D. Pp. 402; 102 illustrations. Philadelphia and London: W. B. Saunders Company, 1909.

THE author's excuse for adding another contribution on malaria to the already long list is a desire to furnish a "practical" work upon the subject, especially adapted to the needs of those who, like himself, are actively engaged in practice in malarial districts. This praiseworthy purpose has fortunately not led him into the error of sacrificing the scientific aspects of his subject; consequently he has produced a reasonably complete and, at the same time, eminently useful book. Although the contributions of other writers must of necessity play a prominent part in the make up of such a book as this, the author's own large experience has enabled him to add many valuable personal observations. The fact that he frequently quotes at length the great authorities upon malaria rather adds to the value of the book than otherwise.

Almost half the book is devoted to a consideration of the etiology of malaria and hemoglobinuric fever. The description of malaria-bearing mosquitoes and their habits is particularly full, perhaps unnecessarily so. The lengthy classification of the mosquitoes of North and Middle America could surely be omitted without seriously detracting from the usefulness of the work. Deaderick's description of the plasmodia of malaria embraces not only the now well-recognized schizogonic and sporogonic cycles of the life history of the parasite, but also includes a description of the rarely mentioned parthenogenetic cycle of Schaudinn. In this connection it may be mentioned that Deaderick is not prepared to accept the evidence recently advanced by Craig, that the parthenogametes result from the intracorporeal conjugation of young asexual forms of the parasite.

In contradistinction to the attention devoted to the other divisions of the subject, the pathological anatomy of malaria is briefly dealt with. The symptomatology and clinical history of malaria, however, are considered in more detail. Deaderick agrees with most modern writers in classifying malaria clinically according to the form of parasite producing the infection. He rightly believes that

it is both confusing and inaccurate to attempt to associate the intermittent type of fever only with tertian and quartan infections, and estivo-autumnal parasites with remittent fever alone. He solves the perplexing problem of a satisfactory division of pernicious malaria by arranging all forms into three groups—the cerebrospinal, the thoracic, and the abdominal. However arbitrary this may be, it at least does away with the usual cumbersome multiplying of names.

The section on diagnosis includes a satisfactory description of the technique of making blood examinations for the malarial parasite. The question of differential diagnosis, although concisely stated, is, upon the whole, entered into sufficiently. The chapters on prophylaxis and treatment are adequate and set forth clearly the essential features of these two important divisions of the subject. It is of interest to note that Deaderick regards methylene blue as the best substitute for the cinchona preparations in the treatment of malaria. At the same time he emphasizes the great inferiority of this preparation to the latter drugs.

Throughout the book that interesting and but little understood condition, hemoglobinuric fever, receives much careful consideration. Deaderick maintains that malaria is “essentially and solely the predisposing cause” of hemoglobinuric fever, and places little credence on the theory that it is a distinctly separate condition due to protozoa other than the plasmodium of Laveran. The most original and ingenious feature in the entire book is the author’s theory of the pathogenesis of black water fever. His hypothesis apparently affords a reasonable explanation for the peculiarities in the occurrence of this remarkable affection.

A word should be said concerning the numerous illustrations, most of which are good. A few of the photographs, however, seem to have more artistic merit than scientific value. Although typographical errors are surprisingly few, it is to be hoped that at the next printing the glaring grammatical slip on the first line of the preface will be corrected.

Taken as a whole, the book fulfils the purpose for which it was written and may be unhesitatingly recommended to all who desire to obtain an accurate conception of the malarial fevers.

G. M. P.

A SYNOPSIS OF SURGERY. By ERNEST W. HEY GROVES, M.S., M.D., B.Sc. (Lond.), F.R.C.S. (Eng.), Assistant Surgeon to the Bristol General Hospital, England. Second edition; pp. 579; 12 illustrations. New York: Wm. Wood & Co., 1910.

THIS volume is an epitome of the salient facts in surgical practice arranged in an orderly and impressive way and far superior to

the general run of such compilations. By means of heavy type and indented margins the reader's attention is rapidly called to the headings and subheadings of the different subjects and ready reference is facilitated. It is impossible to criticise the contents of such a book, and it suffices to state that it closely follows Rose and Carless' Text-book with frequent abstracts from other well-known monographs. It is an excellent book for rapid reference for those who have studied a larger text-book, but is a pitfall without the latter. The volume is small, easy to handle, and well printed.

G. P. M.

AN INTERNATIONAL SYSTEM OF OPHTHALMIC PRACTICE. Edited by WALTER L. PYLE, A.M., M.D., Philadelphia, Member of the American Ophthalmological Society. THERAPEUTICS, by DR. A. DARIER, Paris, translated by SYDNEY STEPHENSON, M.B., F.R.C.S., London, Late Honorary Secretary of the Ophthalmological Society. Pp. 444; 6 illustrations. Philadelphia: P. Blakiston's Son & Co., 1910.

IN the first part of this work upon general therapeutics, following a short chapter upon modern methods of diagnosis, the various means and remedies are reviewed and the indications for their use clearly stated. In the second part, upon special therapeutics, the treatment of the diseases of the different structures entering into the organ of vision, including glaucoma and sympathetic ophthalmia, are discussed *seriatim*. The author's well-known optimism is everywhere in evidence, but this, if not carried too far, is an attribute to be expected and even welcomed in a work dealing with therapeutics. It is, however, considerably toned down and to the advantage of the book in this edition as compared with the lectures as first published. The author still holds to the value of the organic salts of silver, protargol and argyrol, as compared with the nitrate. He thinks that the poor success obtained by some with the former is due to too infrequent application and insufficient strength. He tells us that argyrol, even in 50 per cent. solution, is absolutely painless; "argyrol causes less pain than cocaine or even distilled water."

In extraction of a cataract a preliminary iridectomy is regarded with favor generally, and considered to be definitely indicated in many conditions, such as indocility, or for fear of infective accidents in general maladies (diabetes, albuminuria, etc.). The author recommends allowing the patient to go to his home after extraction with iridectomy, returning when necessary to have the dressings changed. He tells us that this has been his practice in about one-half of the cases operated upon by him for more than twenty years, with results as favorable as when the patients are confined

to the house. Simple extraction, however, should be reserved for hospital treatment.

The translator, Mr. Sydney Stephenson, has, as was to be expected, succeeded admirably in giving the work its English dress. It reads as if it had been written in that language; it is without the ambiguities and strange forms of expression so frequently found in translations.

The editor is to be congratulated upon placing before the profession such an excellent work upon the important subject of ocular therapeutics.

T. B. S.

SURGICAL ANESTHESIA. By H. BELLAMY GARDNER, M.R.C.S., L.R.C.P., London, Anesthetist at St. Mark's Hospital, etc. Pp. 240; 35 illustrations and 12 plates. New York: Wm. Wood & Co., 1909.

THE author states that he has written this book in order to set out clearly for the student and practitioner of medicine principles upon which the art of inducing general anesthesia is founded and the best methods by which the art may be developed. The volume, as a whole, is well written, interesting; and instructive, and, being of small size, presents the subject in a compact manner, and, being free from multitudinous description of apparatus, is rather interesting to read. Unfortunately, the book is marred by constant reference to the testing of the corneal lid reflex in order to ascertain the depth of anesthesia, a procedure which has nothing to commend it and may result in severe injury to the eye. An excellent chapter entitled pathological conditions of the patient discusses those disorders and diseases which affect the exhibition of anesthetics. In discussing the various methods of anesthesia the author confines his remarks to nitrous oxide, ether, chloroform, and ethyl chloride. There is no mention of rectal anesthesia. The discussion of surgical shock is inadequate; the use of nitrous oxide and oxygen as an anesthetic, except for the pulling of teeth, is given no attention, although it is mentioned that there is no physiological time limit to its safe inhalation. The chapter upon anesthesia in operations upon special regions is very inadequate, no mention being made of operations upon the head in which special knowledge is required; nor of various expedients for giving anesthesia when operating upon the tongue, jaws, etc. The book making is satisfactory, although on pages 94 and 95 the figures are very crude.

G. P. M.

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF
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Dioxydiamido-arsenobenzol.—**EHRLICH** (*Deut. med. Woch.*, 1910, xxxvi, 1893), in his address before the *Versammlung deutsche Naturforscher und Aerzte*, September, 1910, gives his observations and conclusions of the treatment of syphilis by arsenobenzol, based on his own work and reports sent him by clinicians of about 10,000 cases treated. The address contains so much that is important that it is impossible to condense it into a few paragraphs; only his conclusions may be referred to. It has been fairly well established that persistence of the spirochetes longer than twenty-four to forty-eight hours after the treatment means that the dose of arsenobenzol employed was too small. Further evidence of the specific action of "606" is seen in the production of antibodies in syphilitics who have received the drug. Their presence is indicated by (1) the curative action of the milk of syphilitic mothers (after treatment) on their infected offspring, and by (2) a similar result obtained by injecting the serum of such patients into luetic sucklings. Injection of "606" into sucklings should not be made until the benefit of the "milk antitoxic" treatment has been secured. A third specific effect is the disappearance of a positive Wassermann reaction after treatment. In certain instances the reverse occurs; a negative Wassermann becomes positive, due to the ultimate effect of the endotoxins liberated when the spirochetes are killed. If a positive Wassermann reaction is unchanged after treatment, the patient should be looked upon as uncured. A negative reaction may mean a cure, or it may mean that the spirochetes which remain are insufficient to yield a positive reaction; their multiplication in time leads to a positive test, indicating a relapse. Again, the almost instantaneous relief from pain, strikingly exhibited in patients with gummas of the tongue or throat, cannot be

explained on anatomical grounds, as it occurs too soon after injection. It must be due to a specific effect of "606." Aggravation of lesions, such as skin eruptions, following injections of "606," Ehrlich looks upon as a manifestation of the Herxheimer phenomenon. It has been observed only after minimal doses of the drug, and is probably explained by the fact that the spirochetes are not killed but are irritated, and thus produce more toxins. Ehrlich warns against the use of "606" in advanced disease of the central nervous system, especially in those presenting cerebral or bulbar symptoms, and also in patients with marked cardiovascular disease. In the former a Herxheimer phenomenon in a positive lesion might prove fatal; in the latter the changes which have already taken place in the heart or vessels cannot be removed. As to the method of administration, Ehrlich finds that intravenous injection leads to the quickest results; robust patients may receive 0.4 to 0.5 gram. The alkaline solution of Alt and Iversen is best for intramuscular injection, but it is rather painful. In neurasthenics, alcoholics, and others who are especially sensitive to pain, or in whom pain leads to cardiac disturbance, the less painful neutral emulsion of Michaelis and Wechselmann is to be preferred. In otherwise healthy individuals, Ehrlich believes the double injection method of Iversen will prove to be the best; 0.4 to 0.5 gram is given intravenously, and then, after two to four days, a subcutaneous or intramuscular injection (the neutral emulsion or the paraffin emulsion of Volk and Kromeyer). The size of the dose should be determined largely by the quality of the patient. He agrees with Alt that in disease of the nervous system the dose should be small—not over 0.4 gram. In the usual syphilitic, especially in the primary stage, larger doses—0.7 to 0.8 gram, possibly more—should be employed (not over 0.5 gram of this intravenously). Ehrlich urges all who employ arsenobenzol to control their results with Wassermann reactions made from time to time, for it is only in this way that the ultimate results of this therapy may be determined. Besides syphilis, "606" has been found to be of great therapeutic value in frambœsia, relapsing fever, sleeping sickness, and malaria. It appears possible that it may be useful in the treatment of smallpox, though at present the experimental stage has scarcely been entered with this disease.

The Intravenous Administration of "606" and its Application Locally.—SCHREIBER (*Deut. med. Woch.*, 1910, xxxvi, 1898) describes a method of preparing arsenobenzol for intravenous injection which he has found satisfactory in over 400 cases. The dose employed should be smaller than that given subcutaneously or intramuscularly; he has found 0.3 gram for women, 0.4 to 0.5 gram for men, to be safe. The drug is placed in sterile water and then *normal* sodium hydrate solution is added. For 0.4 gram of arsenobenzol about 2.8 to 3 c.c. of sodium hydrate is required. If, after vigorous shaking, the solution is not clear, more hydrate is carefully added, a drop at a time, until all the "606" is dissolved. The solution is then diluted to 200 c.c. (150 c.c. or 250 c.c. proved equally suitable) with sterile water or sterile physiological salt solution. (It is understood, as a matter of course, that all the apparatus is sterile.) Before injecting, the solution should be warmed. Care must be exercised that none of the drug is injected into the perivascular tissues, as it is very painful. To determine whether the needle is

within the vein, Schreiber, who employs a needle with a three-way stop-cock, first injects a small quantity of salt solution. After the injection of the drug is completed the tubing and needle are washed out with a few cubic centimeters of salt solution. No pain results from the injection except that produced by the needle, which is negligible. In a little more than 400 patients treated in this way no bad effects have been noted, but vomiting and diarrhoea may ensue if the dose exceeds 0.5 gram. At times there is temporary elevation of temperature, rarely above 40° C. The temperature seldom remains above normal longer than a day. In disease of the central nervous system, especially tabes, the rise in temperature is usually delayed, occurring on the second or third day after injection. Occasionally nausea, vomiting, diarrhoea, and headache were observed, and in one instance urticaria. No ocular or renal manifestations were discovered. In cases in which a second intravenous injection has been resorted to the febrile reaction was less marked or entirely lacking. In treating chancres and condylomas, the author has had very good results from dusting powdered arsenobenzol locally or applying it in the form of a 50 per cent. salve.

Necrosis of the Gluteal Muscles after the Injection of Arsenobenzol.—WECHSELMANN (*Deut. med. Woch.*, 1910, xxxvi, 1910) mentions, among other things, the possibility of necrosis of the muscles after injection into them of "606." He believes that patients exhibit considerable individual variation in susceptibility to muscle necrosis. ORTH (*Ibid.*, p. 1903) reports two cases studied histologically in which such necrosis of the gluteal muscles was found. No local infection was demonstrable by cultural methods, nor was there infiltration with pus cells. One of the patients died six weeks after the injection of "606" from laryngeal carcinoma. Necrosis was still to be seen.

The Treatment of Relapsing Fever with "606."—IVERSEN (*Deut. med. Woch.*, 1910, xxxvi, 1899) has used the Ehrlich-Hata compound in 60 cases of relapsing fever with remarkable results. On experimenting, he found 0.3 gram the proper dose in this disease. Hourly examinations of the blood after the injection demonstrated the complete disappearance of the spirochetes in five to ten hours. With the loss of the organism from the blood, the symptoms disappear and the patient remains well. Thus it is possible with a single dose of the new remedy, arsenobenzol, immediately to arrest the progress of the disease. This result is the more noteworthy since the disease has proved resistant to all previous forms of medication. The author has also had some experience in the treatment of malaria with "606." The patients were studied in the Caucasus. Of 60 cases of tertian malaria treated (0.45 to 0.8 gram intravenously and subcutaneously), 70 per cent. showed no more parasites in the blood after twelve to twenty-four hours. In the remaining cases the parasites persisted in the blood for several days. Only 4 cases of quartan fever were treated; in 2 of these two mild paroxysms followed the injection and then the parasites disappeared; the other 2 cases did not react to the drug. The results in estivo-autumnal malaria were again rather disappointing.

Complement Fixation Tests in Thrombo-angiitis Obliterans.—The pathological study of this condition was published in this journal in October, 1908. It showed that most of the arteries, and sometimes the veins as well, are obliterated over a large extent of their course in the lower extremities. All stages of the occlusive change occur in the various vessels of an extremity or in the same vessel in different parts of its course. The closure is effected by red obturating thrombi; these become organized, vascularized, and canalized. These lesions are not secondary to the gangrene; they may occur without the latter. In short, the condition is initiated by the formation of occlusive thrombi, chiefly in the arteries, but not confined to these, followed by organization or healing, with an attempt at the production of a collateral circulation. This results clinically in pains, ischemia, cyanosis, and trophic disturbances in the affected limb, even extensive gangrene. **BUERGER** and **KALISKI** (*Medical Record*, 1910, lxxviii, 665), realizing that this periarteritis might suggest syphilis, have investigated a series of cases with this in view. The authors and Oppenheimer failed to demonstrate *Spirochæta pallida* in any of the vessels removed from amputated limbs. Nothing definite was ascertained in the histological study to throw light upon the etiology of the process. Clinically, a history of lues in these cases is rarely elicited. Only 2 out of 80 had had a definite syphilitic infection. Twenty-nine cases were examined serologically by complement fixation tests for syphilis. In every one of the 29 the reaction was definitely negative. In only 1 of these could mercurial treatment be considered as influencing the reaction. Buerger and Kaliski conclude that it is fair to assume the disease is probably not of luetic origin.

The Auscultatory Method of Determining Blood Pressure.—In 1905 Kurotkon described the auscultatory method of measuring blood pressure. With the ordinary cuff and manometer, if a stethoscope be placed over the artery below the cuff, avoiding pressure, and the air gradually released, a remarkable cycle will present itself. **GOODMAN** and **HOWELL** (*Univ. Penn. Med. Bull.*, 1910, xxiii, 469) have measured the five different phases of this cycle in figures of pressure on the manometer. With a normal pressure, systolic 130 mm. and diastolic 85 mm., the phases are clear-cut and bear a definite relation to the differences between the extremes of pressure. First, is heard a loud, clear-cut, snapping tone (first phase), due to sudden distention of the vessel walls by the inrush of blood. This persists from the point of systolic pressure for 14 mm. Then follows a series of murmurs, during a drop of 20 mm., the second phase, due to whirlpool eddies produced at the point of constriction of the lumen by the cuff. Suddenly they disappear and a tone which resembles the first is heard. This is the third phase, due to a now well-established stream in the vessel. It lasts for 5 mm., and is followed by a dulling of the sound, for 6 mm., a transitional fourth phase. The fifth phase marks the diastolic pressure. At this point all sounds disappear. Goodman and Howell believe this method to be preferred for simplicity and accuracy. Absence of the fifth phase is pathognomonic of aortic insufficiency. They believe variation in sequence relation of the phase, the recognition of tonal arrhythmias, and irregularities in maximal and minimal pressures will prove of much value in the diagnosis of cardiac neuroses.

Dysentery Carriers.—MACALISTER (*Brit. Med. Jour.*, 1910, ii, 1506) divides carriers into two great classes. The first class consists of healthy persons, who have never suffered from the disease and show no signs of ill health, but nevertheless harbor and scatter the specific organism. In the instance of bacillary dysentery this class is small and unimportant. The author has never found a single case, but Conradi, Collins, and Mayer have been able to demonstrate such conditions in both children and adults living among those affected with the disease. In the second class are people who have had the disease and are thereafter unable completely to eliminate the infection. As agents in the spread of the disease this group cannot well be overestimated in importance. They consist of two groups, in the first of which convalescence is discovered only by the continuation of agglutination. They do not relapse, but they harbor infection somewhere, and an occasional stool contains mucus. The second group is of relapsing and chronic cases, a constant source of infection. Macalister emphasizes the need of isolation, observation, and care during convalescence as a means of prevention of spread of an epidemic. Unfortunately, these incomplete convalescents form a high proportion of the cases.

The Parathyroid Glands and Sudden Death.—As a cause of sudden death in children, not a few cases of status lymphaticus have been recorded. But it often happens that necropsy reveals no adequate cause of death. GROSSER and BETKE (*Münch. med. Woch.*, 1910, lvii, 2077) report 3 cases which would fall in the latter category, had they not carefully dissected and examined the parathyroid glandules histologically. In all their cases no lesion sufficient to cause death was found, aside from the changes in the parathyroids. In 2 cases they found only three glandules—all hemorrhagic. In the remaining case all four glands presented fresh, extensive hemorrhages. Similar lesions were not discovered in other organs. From a study of the literature, they find that more than one parathyroid gland must remain intact to preserve life. They believe, therefore, that the lesions they found in these glands are quite sufficient to explain the death of the patients, and urge the necessity of their careful examination in cases which are obscure. The patients died with spasms.

Anemia and Hemolytic Icterus of Tuberculous Origin.—LANDOUZY (*Presse médicale*, 1910, 761) reports the case of a young man, aged thirty-eight years, with pulmonary tuberculosis. The man had a severe grade of anemia—red blood corpuscles, 1,050,000, and hemoglobin, 10 per cent. The spleen was enlarged. The conjunctivæ were subicteric, and the urine highly colored (urobilin). A diminution in the resistance of the red blood corpuscles was demonstrated (0.54 per cent.). As many as 25 per cent. of the red cells showed granules on vital staining, and the nucleated red cells amounted to 35 per cent. The patient's serum contained neither isolysins nor autolysins. After a time, under treatment, the signs of infection regressed, with a similar change in the anemia and icterus. As the pulmonary lesions seemed to become stationary, the fragility of the red blood cells disappeared. This parallelism of the hemolytic syndrome and the infection and the absence of any other cause leads Landouzy to believe the hemolytic jaundice dependent

upon the tuberculosis. It is known that acquired hemolytic jaundice is met with under various circumstances. Malaria, syphilis, and cancer are among the known conditions in which this syndrome has been met with. The author believes his own observation to be the first in which the hemolytic condition evolved in the course of tuberculosis. It supports the hypothesis of the bacillary origin of certain of the hemolytic syndromes.

Typhoid Fever Statistics.—SALLOM (*Med. Record*, 1910, lxxviii, 625) states that from January, 1898, until June, 1909, there occurred in Philadelphia 68,943 cases of typhoid fever. Of this number, 8102 died, a mortality of 11.75 per cent. It is well known that season affects the prevalence of typhoid fever. These statistics show, without doubt, an influence upon mortality also. Starting with a mortality of 10 per cent., it rises during February and March up to 12.37 per cent. Falling during April, it ascends again in May and June. The July mortality is phenomenal, reaching the maximum of 17.61 per cent. Dropping as precipitately as it rose, the mortality of August and the rest of the year varies between 10.21 and 11.75 per cent. On the other hand, morbidity is highest in January and February and lowest in the fatal month of July. Likewise, in September, when the second maximum of morbidity occurs, a second minimum in mortality is obtained. The point is made, however, that a patient dying in January, for instance, probably contracted the disease in December, in the majority of cases. Therefore, Sallom constructed a second chart, in which the mortality for any month was considered with the morbidity of the preceding month. This collaborates the first figures. With the minimum morbidity of July the first maximum in mortality is present; and with the second maximum in morbidity, occurring during September, the minimum mortality is obtained. Sallom concludes that with the maximum morbidity a minimum percentage mortality is present, and *vice versa*; and, further, as morbidity falls mortality rises.

S U R G E R Y .

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The Operative Treatment of Penetrating Wounds of the Diaphragm.—MAGULA (*Archiv f. klin. Chir.*, 1910, xciii, 581) collected from the literature 129 cases of penetrating wounds of the diaphragm which had

been operated on, and adds 61 new cases. There were 64, but 3 did not come to operation. In the great majority of the cases the wound comes by way of the pleural cavity. In a very large number wounds of the breast and of the abdominal organs are associated, in Magula's cases in 59 per cent. It is incontestible and recognized nearly everywhere as axiomatic, that expectant treatment in these cases is not to be recommended, for the following reasons: (a) There is always the danger threatening the occurrence of and the strangulation of a diaphragmatic hernia. (b) There exists also the danger that the wound of an organ, the breast or an abdominal organ, will be overlooked and the patient die of internal hemorrhage or peritonitis. Since, on the other hand, the diagnosis of a wound of the diaphragm before operation is especially difficult, and, according to Magula's experience, in about 40 per cent. of the cases impossible, because of the absence of the characteristic signs, the view is gaining ground that every penetrating wound of the thorax or abdomen, not more than twelve hours old, should be enlarged and explored. Magula's experience strongly supports this view. The operation of choice for all cases is by the pleural route. Only in rare cases must the combined method, thoracolaparotomy, be employed. If the closure of the wound of the diaphragm is impossible, the pleural cavity should be isolated, that is, the edges of the diaphragmatic wound should be sutured to the costal pleura. In this way a diaphragmatic hernia is prevented and the avenue for infection of the delicate pleura is shut off.

Arthritis Deformans in Children.—PERTHES (*Deut. Ztschr. f. Chir.*, 1910, cvii, 111) says that the examination in one case showed that while flexion was free, abduction, adduction, and rotation were completely abolished. The trochanter was 1 cm. above the Roser-Nélaton line. There was no pain on movement or pressure and the x-rays showed it was not a case of coxa vara. The angle of the femoral neck was normal and the head cone-shaped rather than globular. Observation during a year gave further indications of the existence of an arthritis deformans. Within a year Perthes saw not less than 6 similar cases. Von Brunn, in 1903, collected 38 cases from the literature, 26 occurring on one side and 12 being bilateral. The frequency and practical importance of this condition in children is greater than has been thought up to the present time. In the greater number of cases trauma does not occur. There is no reason to ascribe the cause to asymmetry of the body. In one of Perthes' cases the condition originated in a bacterial inflammation of the hip-joint, although the first sign appeared only after a symptomless interval of several years. The first pathological change is often a flattening of the epiphysis of the head, which frequently results in a cone-shaped deformity of the head. The gradual change in its shape can be shown by a series of skiagrams, which also indicate disturbances in nourishment within the epiphysis and the development of subchondral foci of absorption. The limitation of movements is the direct mechanical result of the formation of the joint. Pain is not produced by active or passive movement. Spontaneous pain, on the other hand, occurs especially after long-continued walking, and not rarely is referred to the knee. Yet there occur cases in which, notwithstanding a high grade of deformity, pain of all kinds is completely absent. Crepi-

tation can be demonstrated only in a small portion of the cases. Lameness, which is, as a rule, the first symptom of the condition, is due, as in congenital luxations and coxa vara, to insufficient abduction. Confusion in diagnosis between arthritis deformans, coxa vara, and tuberculous ostitis is to be expected. In those cases which have been watched for a long time the pathological changes progressively advance. At times, however, the limitation of movement and spontaneous pain may be improved. In the treatment immobilizing bandages are to be avoided. Systematic passive movements and massage are to be recommended. For the cases with far-advanced bone changes, operative treatment should be considered. This may consist of operative modelling of the head or of resection.

Tenomyoplasty in Inguinal Eventration.—JACOBOWICI (*Deut. Ztschr. f. Chir.*, 1910, cvii, 289) did the following operation on a left-sided inguinal eventration in which the hernial aperture admitted four fingers. An incision was made, beginning at the outer side of the thigh, about 15 cm. below the anterior superior iliac spine and extending upward to just below the spine. From this point it was carried across the abdomen about to the linea alba. The flap thus outlined was turned downward and inward, exposing widely the field of operation. An incision was then made in the sheath of the rectus, parallel to the median line, from the pubis to the upper part of the wound, and continued at right angles from the upper end of this incision outward almost to the outer edge of the rectus muscle. This flap of the rectus sheath could be turned downward. The inguinal canal was then opened by a slightly curved incision extending from the anterior superior spine to the external ring. In this way a second flap was obtained from the external oblique aponeurosis, with its base at Poupart's ligament. There was no hernial sac present, but if there were it could be handled as in the ordinary Bassini operation. The edge of the flap from the rectus sheath was then turned downward and sutured over the hernial region to the edge of Poupart's ligament. Over this the flap from the external oblique was sutured, thus covering the hernial region with two aponeuroses. The sheath of the sartorius was then opened by a longitudinal incision and the muscle divided transversely at the junction of its upper and middle thirds. After suturing the end of the distal portion to its sheath, the proximal upper third of the muscle was freed from its bed and laid over the hernial region, where it was fixed with sutures, the cut end lying over the exposed surface of the rectus muscle. The sheath of the sartorius was then closed by a continuous suture, and the skin wound closed. A strong abdominal wall was thus obtained and there were no disturbances in walking from the division of the sartorius.

The Functional Cure of Paralysis of the Trapezius by Means of Detached Portions of Fascia.—ROTHSCHILD (*Zentrbl. f. Chir.*, 1910, xxxvii, 1441) says that while the serratus magnus, by turning the scapula on its long axis, continues the abduction of the arm after the horizontal has been reached, upon the trapezius falls the task of holding the bone in its normal position. This permits the serratus to come strongly into action. If, in a case of paralysis of the trapezius, while an attempt at voluntary abduction of the arm is being made, the scapula is pressed

toward the spine and toward the feet, thus placing it in its normal position, the disturbances in the movement of the arm disappear immediately. This manual pressure can be substituted by operation, through a pull in the opposite direction. A free exposure of the field of operation is obtained by an incision from the superior vertebral angle of the scapula, downward to the first lumbar vertebra. A piece of the fascia lata is taken, about 20 cm. long and 4 to 5 cm. wide. One side of the narrow end is fixed by sutures to the vertebral border of the scapula, and while an assistant presses the scapula toward the spine, and downward, the other side is sutured under strong tension to the latissimus dorsi and deep muscles close to the spine. In order to prevent the adhesion of the fascial strip to the overlying skin, it is placed under the trapezius muscle. In a case so treated, in which the paralysis had existed half a year, and had rendered the patient completely unable to work, in ten days he was so improved functionally that neither he nor his physician could see any difference between the affected and normal sides. Cosmetically, the improvement was marked.

Contraindications to the Intravenous Infusion of Saline Solutions.—BERTELSMAN (*Zentrbl. f. Chir.*, 1910, xxxvii, 1417) says that König has twice seen death hastened by large intravenous infusions of saline solutions. He had previously strongly recommended them, and the present paper was written chiefly to meet the objections of Heineke and others to them. Heineke says that they are strongly contraindicated in peritonitis cases in which occur disturbances of circulation from paralysis of the vasomotor centres. In these cases the heart is deprived of blood because the greater part of the latter is retained in the relaxed abdominal vessels. Bertelsman believes that by filling up the whole system of bloodvessels a quantity can be introduced which will compensate for the relaxation of the abdominal vessels. The heart will thus be filled and after some time the circulation will return approximately to the normal. In this way favorable operative conditions will be produced. That this hope is justified he has proved many times. It has been shown that in peritonitis we do not have to deal with the bacterial contents of the blood, since surgical peritonitis, as a rule, is not a general infection. It is well known that saline solution impairs the bacterial properties of the blood, and that therefore it should not be employed in general infections. When there already exists weakness of the heart, one should proceed with more care. In severe pneumonias, since the bacteria are circulating in the blood, the disturbances of the circulation can best be combated by small quantities of saline solution with adrenalin added.

Operation for Exstrophy of the Bladder.—FINK (*Zentrbl. f. Chir.*, 1910, xxxvii, 1467) refers to the ingenious operation of Makkas, in which a new bladder was made of the isolated cecum, the ureters implanted into it, and the appendix used for a urethra (for abstract, see this journal, 1910, cxi, 761). Fink did an operation in which, after closing the ectopic bladder, he used the appendix to conduct the urine from the bladder to the cecum. It consisted of the following steps: An incision was made along the junction of the bladder and the skin and including the remains of the urethra. The bladder wall was then separated down to the ureters, which were catheterized. The peritoneum was

opened in the upper part of the circumference of the bladder and the appendix was located and brought into view. It was 6 cm. long and was divided transversely near its peripheral end. The canal was then irrigated with water toward the cecum to cleanse it and establish the permeability and caliber of its canal. The bladder opening was closed by suture of the muscularis and mucosa to the upper pole. A perforation was made into the bladder at its deepest part and the end of the appendix introduced through it and sutured in place. The mesentery of the appendix was sutured to the bladder to fix it more securely. The remaining opening was then closed. The patient died, so that the functional results could not be shown. The following advantages are advanced for the operation: The bladder is formed of tissue anatomically and physiologically normal. The normal valves of the appendix prevent the entrance of gas and feces, as after the Maydl operation, when the ureters are transplanted into the sigmoid. If infection should occur, the appendix could be conducted to the surface by a second operation.

Figures about Fractures and Re-fractures of the Patella.—CORNER (*Annals of Surgery*, 1910, lii, 707) collected the statistics of cases of fractures of the patella admitted to St. Thomas' Hospital during the years 1890 to 1907, inclusive. There were in all 504 cases, and of these, in 55 re-fracture occurred. The most important points which they show are summarized as follows: Fractures in the lower half of the patella are the most frequent (83 per cent.). Triangular-shaped patellæ are the most common; oblique-shaped patellæ come next. Transverse fractures are the most frequent; comminuted fractures come next. Three males fracture their patellæ to one female. Fractures of the right patella are a little more frequent than of the left. Two underwent operation to every one that did not. Fracture of the patella is most frequent between the ages of thirty to forty years. It is the most frequently re-fractured bone in the body. After operation, 69 per cent. of re-fractures occur in the first year after the injury. After treatment other than operation, 86 per cent. of re-fractures occur after the first year. The percentage frequency of re-fractures is approximately the same after operative as it is after non-operative treatment. The advantages of operation are solely in the quick and complete recovery of the function of the limb.

Surgery of the Thorax.—QUINBY (*Surgery, Gynecology, and Obstetrics*, 1910, xi, 482) says that by the intratracheal insufflation method of operation of Meltzer and Auer we can now create a situation corresponding to that of internal respiration, in which the dangers of pneumothorax are entirely overcome. It is the simplest method known which will "breathe for the patient." Other methods have allowed carbon dioxide slowly to accumulate in the air passages, and finally endanger the heart. By this new method it is very hard or even impossible to give sufficient ether to kill. Its only disadvantage is the necessity of intubation of the trachea, with possible danger of pneumonia from this source. The evidence which we have thus far tends to show that this danger has been much overestimated. In none of the cases in which the method has been applied to man has bronchitis or pneumonia occurred.

In so far as Quinby's experimental observations go, they entirely confirm the much greater experience of Meltzer, Carrel, and Elsberg, who find that the method of intratracheal insufflation is very safe, and rests on a firm physiological basis. In some thirty observations, some of them as long as four hours, others during such severe operations as total right pneumectomy and œsophageal sutures, Quinby has never had a death due to the method of anesthesia. The apparatus is about as easily carried as the usual Bennett inhaler kit, so that with it every surgeon has at his command an arrangement for making operative pneumothorax harmless. Of moderate price, easily transportable, and safe, it should make operations on the thorax common, and done by many surgeons, instead of, as today, by only a few. Further than this, it places at his command an apparatus which will "breathe for the patient" in case of respiratory failure from many causes other than acute pneumothorax. Already it has been used with success in cases of myasthenia gravis, severe opium poisoning, and cessation of respiration from brain abscess, as well as in the operative cases. It is Quinby's hope that many surgeons will familiarize themselves with the principle underlying this method, as it is one which will undoubtedly be of great value in the development of thoracic surgery.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Use of a Salt-poor Diet.—LEVA (*Med. Klinik*, 1910, vi, 782) gives a review of the literature dealing with the different indications for a salt-poor diet. He then discusses more particularly the practical application of such a diet and gives valuable tables showing the salt content of various articles of food based upon 360 analyses. There are included in his tables many foods poor in salt content that serve to make a liberal mixed diet in cases in which abstention from salt is indicated. These tables should be consulted for details, as only general statements are given here. Meat is the one article that seems to require considerable salt to render it palatable. In general, beef, veal, pork, and fish require more salt than poultry to render them palatable. Some of the meat foods contain a higher percentage of salt to start with. Butter sauces, and sauces with egg-yolk, oil, vinegar, lemon, etc., will take the place of salt if given with many of the meat foods. Eggs may be used to supply protein as they contain only a small percentage of salt. Soups and meat extracts require large amounts of salt to render them palatable. Vegetables are, as a rule, low in salt content with the exception of celery, carrots, savoy, spinach, cauliflower, and some varieties of winter cabbage. Bread should be made without salt and eaten with sweet butter. Some varieties of cheese contain a high percentage of salt, while

others are poor in salt. Most of the mineral table waters contain a large percentage of salt. Cocoa, milk, malt beverages, tonics, coffee, tea, etc., are low in their salt content. Cereals form an important part of the salt-poor diet as they contain only small amounts of salt. Cream and sugar can be freely used. Both fresh and cooked fruits may be taken in abundance. Canned goods should be excluded as they usually contain a considerable amount of salt. Leva says that horse-radish, mustard, and vinegar may be used to disguise the lack of salt in a salt-poor diet.

Alum Baths in Typhoid Fever.—BOGGS (*Jour. Amer. Med. Assoc.*, 1910, liv, 2124) says that for two years alum baths have been used as a routine method of treatment in the wards of the Johns Hopkins Hospital, with a reduction of 50 per cent. in the incidence of such skin complications as boils, abscesses, dermatitis, bed sores, etc. The procedure is very simple and is carried out as follows: One pound (500 grams) of powdered alum is quickly dissolved in a little hot water and added to the tub during the filling. With the average tub of 450 to 500 liters, this makes approximately a 1 to 1000 solution. The cost is about 4 cents per bath. The patient is bathed in the alum solution just as in ordinary water and experiences no inconvenience from the presence of the drug. The only noteworthy changes in the skin are a slight increase in desquamation during convalescence and a decided diminution in the incidence of skin complications of all sorts. In these cases the care of the skin is the same in all except for the alum baths. It is not suggested that the alum baths can replace the rigid care of the skin in the ordinary way, but that with them the frequency of skin complications will be still further reduced.

Antityphoid Vaccination.—HARTSOCK (*Jour. Amer. Med. Assoc.*, 1910, liv, 2123) believes that antityphoid vaccination by means of the injection of dead typhoid bacilli is now destined to be a practical measure of prophylaxis and of value in the handling of typhoid epidemics. He says that in promulgating this vaccination as a popular measure it is necessary to convince the patient as to its immediate benign effects. The layman must be assured that there will be no detention from business and that the injection is without harm. The military commander, in times of war, when troops are being mustered in, must be convinced that his forces will be ready for duty at any time. Hartsock reports a series of 1100 vaccinations that, according to him, give sufficient evidence to assure affirmatively both the above. He advises antityphoid vaccinations for the following classes: (1) All persons between the ages of fifteen and twenty-five. Osler states that the greatest susceptibility to typhoid is between these ages. (2) All persons exposed in time of an epidemic. (3) Nurses and physicians. (4) All persons in the military service, and more particularly in time of war, when troops are enrolled and concentrated in camps.

The Treatment of Amœbic Dysentery.—AXISA (*Therapie d. Gegenwart*, 1910, li, 263) says that the usual methods of treating amœbic dysentery are most unsatisfactory. Ipecac, which is considered a specific by many, has the marked disadvantage of causing vomiting, or

at least nausea. High irrigations are too painful to be of use in the acute cases, although valuable in the treatment of subacute and chronic cases. Axisa calls attention to a remedy introduced by Legrand under the name of kossam. This remedy has been used in a crude way by the natives of tropical countries as a cure for dysentery for some time. It may now be obtained in tabloid form. Axisa has used it and speaks very highly of its good effects. The most striking effect is in the rapidity with which the blood disappears from the stools. He ascribes a hemostatic action to the kossam, and has also used it with success in profuse hemorrhages in intestinal tuberculosis and bleeding hemorrhoids. In addition, this remedy also seems to exert a direct action upon the amœbæ. Of 37 stools that were examined, no amœbæ could be found after treatment lasting from eight to ten days. Kossam is not astringent, and as the blood disappears from the stools it is advisable to add intestinal astringents to the treatment. When the process becomes subacute, high irrigations with a 0.5 or 1 per cent. solution of tannin will hasten the cure. He gives the details of a number of cases treated by this method, and says that he has seen a number of cases completely cured in three weeks, a result that could only be obtained in from six to eight weeks by former methods of treatment. For the treatment of subacute and chronic dysentery he advises, in addition to kossam, high irrigations of either a 1 per cent. ichthyol solution or a 0.5 to 1 per cent. solution of tannin. He also advises an occasional purge of sodium sulphate, and finally, when amœbæ are no longer found, the administration of such astringents as bismuth or tannin until there is no longer any diarrhoea.

Vaccine Therapy in Tuberculosis.—KING (*New York Med. Jour.*, 1910, xcii, 164) says that for the present vaccine treatment in tuberculosis consists in, first, the treatment of the tuberculous infection itself by some one or more of the tuberculins; and second, the treatment of the secondary pyogenic infection by the specific bacterial product indicated by the character of the secondary infection. He believes that there is no especial advantage in the use of autogenous tuberculins. On the other hand, the comparative ease of preparation and standardization of autogenous bacterial vaccines to meet the requirements of the usual secondary infection, renders their use both practical and preferable. At the Loomis Sanitarium two classes of patients are advised to take tuberculin: (1) The class of incipient cases which have been under observation for a sufficiently long time to justify the belief that they are not progressive and are without fever or other evidences of a marked general toxemia. (2) The class of more advanced cases, presenting evidence of "arrested" activity, the patients having been for some time without material change in their condition, either local or constitutional, but who still have cough and tubercle bacilli in their sputum. King thinks that the choice of tuberculin is more a matter of arbitrary preference on the part of the physician than of advantage on the part of any particular tuberculin. He prefers bacillus-emulsion in most cases, though giving no reason for this choice. At the Loomis Sanitarium, as a routine practice, they begin with 0.00000001 gram (solid substance) of bacillus-emulsion and 0.0000001 c.c. of bouillon filtré, and proceed by 50 per cent. increases until 0.0001 gram, or 0.00001 gram in the case of bacillus-

emulsion, and sometimes larger doses in case of bouillon filtré are reached; afterward proceeding at the rate of 20 per cent. increases until the maximum dose or the termination of the course is reached. However, should intolerance for an increased dose develop at any time during the treatment, this plan of progression may be wholly changed. No attempt is made to attain a definite maximum dose. It is rare to exceed a maximum dose of 0.001 gram of bacillus-emulsion and 0.1 to 0.5 c.c. of bouillon filtré at the end of a course of from seven to nine months. King thinks it safer to give the tuberculin at intervals of one week, though it is no doubt safe to give the tuberculin twice a week during the earlier stages of the treatment. General reactions are to be avoided, but King thinks that local reaction may be actually advantageous in some cases. In young persons, when the superficial lymphatics are the only demonstrable foci of infection, a reaction characterized by some swelling and tenderness in the infected glands is almost always followed by a distinct improvement. This also seems to be the case in some laryngeal cases, though in those cases in which an old fibroid infiltration has already appreciably narrowed the glottis, a focal reaction may undoubtedly cause a sudden and very alarming stenosis. Such a lesion, according to King, contraindicates tuberculin treatment. King has also treated cavity cases with persistent high fever that does not yield to complete rest in bed with autogenous vaccines prepared from the patient's sputum. He gives the method of preparation of such a vaccine, and states that no untoward effects have occurred as a result of this treatment. He thinks that a relation can be traced between this treatment and a remission in the symptoms, chiefly in lowered temperature in the majority of cases so treated. However, the number of cases treated has been too few to admit of any positive statement as to the value or the practicability of this method of treating the complicating pyogenic infections in pulmonary tuberculosis.

The Tuberculin Treatment of Pulmonary Tuberculosis in Office and Dispensary Practice.—MILLER (*New York Med. Jour.*, 1910, xcii, 160) says that the present position of tuberculin therapy may be summarized as follows: (1) Tuberculin is a valuable addition to our means of treating pulmonary tuberculosis, its effects being best evidenced by a greater permanence of good results, a larger proportion of cases which lose bacilli from their sputum, and the relief from toxic symptoms, especially in chronic advanced cases. (2) Tuberculin can do no harm when given carefully in proper dosage. (3) No one of the ordinary preparations of tuberculin possesses any material advantage over the others. (4) The so-called clinical method is the most practicable guide for the administration of tuberculin in pulmonary tuberculosis, and the aim should be to produce no general reactions. (5) The time element in treatment is more important than the absolute dosage, the latter varying with every case and the former being never less than six and often more than eighteen months. (6) With unimportant modifications, this method of treatment is quite as applicable to dispensary and office patients as to those in sanatoria.

The Treatment of Gastric Subacidity with a Coarse Diet and Lemon Juice.—ROEMHELD (*Therapie d. Gegenwart*, 1910, li, 285) says that it is a well-known fact that coarse foods exert a greater stimulating action upon the gastric secretions than do foods that are finely divided. Thus it is customary to give patients with gastric hypersecretion food in the form of soups or purées in order to diminish the acidity. Roemheld has observed that in patients with a diminished acidity but with unimpaired motility it was possible to increase the acidity by giving coarse foods such as graham bread, fruit, cereals, salads, etc. This same effect was observed in cases of lowered acidity of nervous origin, and in gastritis with low acidity and an increase of the secretion of mucus. He believes that the coarse food excites mechanically the production of gastric juice, cleanses the mucus from the stomach, and counteracts constipation, which is so often associated with subacidity. Roemheld also believes that there are many patients who are not able to take hydrochloric acid. He advises giving such patients citric acid, especially in the form of lemon juice added to salads.

Observations Concerning the Action of Digitalis.—VON LEYDEN (*Therapie d. Gegenwart*, 1910, li, 482) deprecates the tendency to prescribe digitalis as soon as symptoms of cardiac incompetence occur. He says that tolerance soon follows the use of digitalis, and when more serious symptoms of cardiac failure develop, no results are obtained from its administration. Measures tending to secure both physical and mental rest for the patient should be employed before the use of digitalis. Von Leyden is of the opinion that digitalis has a greater action upon the left side of the heart, and so may fail to benefit those patients suffering more from a failure of the right heart. In fact, he believes that digitalis may even be harmful in these cases. He also thinks that, due to the action of digitalis principally upon the cardiac muscle, there will be little or no effect in advanced myocarditis or when valvular disease is associated with myocarditis. Von Leyden has not seen much benefit derived from the use of digitalis in fever; in fact, large doses seem to be actually harmful. He prefers the infusion of digitalis, and gives it in smaller doses than those usually prescribed, and discontinues it when its therapeutic effects have been obtained. He believes that digitalis in pill form is untrustworthy and that the tincture is uncertain. Digitalis leaves vary in strength according to where grown and the time of gathering. Age also diminishes their strength.

The New Treatment of Syphilis (Ehrlich-Hata).—ELSNER (*Jour. Amer. Med. Assoc.*, 1910, lv, 2052) says that his experience with this remedy as he saw it used abroad and in his private and hospital practice justifies the following conclusions: (1) The treponema, otherwise known as the *Spirochæta pallida*, is positively destroyed and the living contagion of syphilis is promptly removed by the Ehrlich-Hata remedy. (2) The preparation "606" promptly and favorably affects visible and palpable syphilitic lesions. It also removes deep-seated gummas. (3) The remedy stays the destructive and onward march of syphilitic ulcerations and causes their healing in a surprisingly short time. (4) It is more rapid in its effect on specific disease than any other known remedy,

(5) It is likely to prove more valuable than any other remedy in the treatment of the specific diseases of most internal organs. (6) It cannot replace cicatricial tissue; neither does it affect favorably chronic degenerative diseases of the nervous system, such as paresis, system diseases of the cord, in which there is a break in the continuity of nerve structure, though in some cases it seems to influence favorably the continuous crises of locomotor ataxia. (7) In all cases it causes a leukocytosis and the formation of antibodies. (8) It materially modifies, and in most cases ultimately negatives, the Wassermann reaction. (9) It unquestionably floods the circulation with endotoxins resulting from the death of millions of spirochetes, and in all probability an antitoxin is developed in the blood serum. These facts must be thoroughly considered in connection with the treatment. (10) In acute and threatening deposits in vital organs the effect of "606" will often prove life-saving, because of its prompt action, and for that reason it is preferable to the iodides of mercury. (11) It ought not to be given to ambulatory patients; neither is it safe in the hands of the careless or those who have not seen it used and learned the difficult method of its preparation for injection. (12) The hospital, where all things required in the preparation of the mixture of "606" can be sterilized, and where the centrifuge can be used, is preferable to any other place for its injection. (13) Patients injected should be kept quiet and in bed during seven days under close observation, and for a longer period if indications demand. (14) Second injections, if indicated, should not be given in less than eight weeks after the first. (15) Contraindications should be carefully considered before using the remedy. Patients with any other infection than that of syphilis should not be injected, however mild the former may be, until a safe period has elapsed after their recovery; neither should the feeble or old or those with any other syphilitic organic disease be injected. (16) Congenital syphilis can be cured by injecting the mother of the nursling with "606," without direct treatment of the child. Mierowsky and Hartmann have used the blood serum of injected mothers in the treatment of congenital syphilis with decided benefit. (17) The living contagion is destroyed by "606," hence its early cure can prevent the spread of syphilis. This subject demands the immediate attention of sanitarians and those directly interested in public health. (18) In occasional well-selected cases the use of the iodides after the method of Wechselmann will increase the efficacy of "606" when second injections are necessary. From two to three weeks should lapse after thorough mercurial treatment, when this has been used, before the injection of arsenobenzol. (19) In spite of the fact that nearly all agree that the effect of arsenobenzol is magical, sufficient time has not elapsed to justify the conclusion that a single injection of "606" will prevent what we now recognize as the secondary and tertiary stages of syphilis. Only after long years of careful observation shall we be able to reach a positive conclusion. It will be necessary, therefore, to keep injected patients under close observation.

PEDIATRICS.

UNDER THE CHARGE OF

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The Causes and Management of Eczema in Infants.—DR. GALEWSKY (*Medizinische Klinik*, 1910, vi, 1855) declares that eczema is the most important skin disease of infancy and constitutes half of all skin affections in that period. He notes the principal types, such as seborrhœa of the head, involving the entire face; large, sharply defined patches on the chest and back; small isolated seborrhœic patches, usually on the face; eczema intertrigo; damp, crusty eczema, with great skin thickening, in lymphatic infants; and the more disseminated, dry eczema in anemic infants. It was recognized long ago that excess of foodstuffs over the amounts necessary and assimilable was a factor in producing eczema. Bohn has laid especial stress on excess of fats in this connection. But the foundation for the production of eczema lies in a constitutional susceptibility or diathesis, called lymphatic constitution, lymphatic diathesis, exudative diathesis, etc., which is characterized by enlargements of the lymphatic system, pallor, catarrhal affections of the respiratory tract, and a great tendency toward skin affections. The majority of children of this type are eczematous, and a correction of their diet and an alteration of their diathesis by treatment is followed by improvement or disappearance of the eczema. Galewsky does not believe in a scrofula of infancy as such, but holds such conditions to be an exudative diathesis, which later in life furnishes the soil upon which tuberculosis develops. Errors in the chemical combination of food, hereditary disposition without diathesis, and uncleanness are also predisposing factors. Eczema follows many other primary skin affections. Galewsky has never seen severe constitutional disorders follow sudden healing of an eczema, which, Henoch claims, does occur. Internal treatment relating to nutrition and food must be combined with external measures to secure good results. Apparently healed eczemas often leave unnoticed areas of skin thickening which cause a recurrence when nutrition is again disturbed. The infant's food must be reduced to just that amount which can be assimilated and which will maintain body weight. Regular feeding intervals, regular weighing on scales, and careful observation of the general development are very important. Especial stress is laid on reducing the fat percentage in the food to a minimum, and making three of the five daily feedings weaker in proportion than the other two. Eggs, cream, and butter should be entirely avoided. In older children vegetables should be substituted in the diet as early as possible. Fresh air, sunshine, and change of environment are often important factors. Overfeeding and an excess of fats are common faults in anemic infants, in whom regulation of the bowels is highly important. In some cases feeding with whey, as in Finkelstein's method, gives good results. Arsenic is of use in a small number of protracted cases only. In gastric disorders he mentions

intestinal antiseptics, such as ichthalbin, calomel, benzonaphthol, bicarbonate of soda, and magnesia. Local treatment consists of cleansing the skin with lotions not containing soap and in preventing scratching. Later, mild sulphur baths are recommended. He uses powder for moist eczema, or cloths damp with a resorcin solution. Dry eczema calls for soft ointments of diachylon, lead, zinc, bismuth, and salicylic acid. For eczema of the head he uses salicylic acid ointment, chamomile washes, and, later, tar ointment.

The Presence of Bacterium Coli on Out-of-door Objects, Especially on Food—GEORG NEUMANN (*Deut. med. Woch.*, 1910, xxxvi, 2046) has proved the presence of *Bacterium coli* on the equipment of kitchens and outhouses which was constantly being touched and handled by human hands. He undertook a second investigation on foodstuffs and fruits. The Eijkmann method was used in both investigations: The *Bacterium coli* was found present and identified, in two out of five, on loaves of bread; once in eight times in wheat; eight times in eight different samples of milk; and two out of four times in butter—the specimen being taken from the centre of the mass. Fruits tested—apples, pears, plums, and grapes, bought from hucksters—all showed positive results, and *Bacterium coli* was identified in four tests on apples, and positive three times in four tests on pears and plums. The result was practically the same on fruits bought in market from farmers. Apples, pears, and plums which showed *Bacterium coli* were given to a maid to be washed under a spigot, and then the fruit was again tested. The two apples showed *Bacterium coli* after washing; of the two pears, one only was negative after washing, but both plums were negative after washing. This test was repeated, with practically the same result, on fruits from a different source. *Bacterium coli* was isolated and identified in all the positive tests. In tracing the method by which *Bacterium coli* reached the fruit, Neumann found the following facts: The ground underneath and near the trees bearing the fruit showed the presence of *Bacterium coli* in all of ten examinations, but as the fruit was practically all picked from the trees, and did not reach the ground, Neumann took cultures from fruit still on the trees, on a hot, dusty day, to test whether or not the dust conveyed *Bacterium coli* to the fruit. In the fifteen examinations thus made, including many cultures from fruit in several orchards, not one was found positive. This conclusively showed that the fruit was contaminated by the hands of the hucksters and dealers. Grapes seem the only exception, since four examinations on grapes bought from hucksters were negative, and five examinations of grapes still on the vine were also negative. The tests on drinking water were negative. Neumann points out the dangers of epidemics through the infection of the intestinal tract from fruits and also other food, grapes being apparently an exception. From his investigations he predicts it safe to eat fruit personally plucked from the trees. He claims that wherever the human hand is laid there *Bacteria coli* may be found.

Acute Laryngeal Dyspnoea in Children.—HAROLD BARWELL (*Lancet*, 1910, clxxxix, 447), in a clinical lecture under this heading, makes the following points: Laryngeal obstruction is more common in children

because the lumen of the glottis is absolutely and relatively smaller. The principal reason is the tendency to spasm of the glottis in the early years of life. Spasm is a most important factor in nearly all forms of laryngeal obstruction. In the diagnosis of laryngeal dyspnoea the following points are noted: Inspiratory stridor is marked, while expiration is easy. If the larynx is obstructed, that organ is forced downward distinctly with each inspiration, which effect does not occur in obstruction elsewhere. The head is thrown back to open the laryngeal region. The causes of laryngeal dyspnoea range from pure reflex spasm of the glottis to simple mechanical obstruction. Pure spasm is caused by reflex irritation, as in laryngismus stridulus, and is a combination of morbid excitability of the nervous system plus reflexes from the bowel, etc. In acute laryngeal affections the reflex irritation is due to catarrhal inflammation. In laryngeal diphtheria, primary deposits of membrane are very rare. Non-diphtheritic, membranous laryngitis in children, aged from two to eight years, is generally primary in the larynx and is accompanied by a loud ringing cough, followed by spasm, fever, and dyspnoea. This form is more dangerous than the diphtheritic, since the advent of antitoxin. Marked dyspnoea between exacerbations usually means oedema or diphtheritic membrane. Retropharyngeal abscess and foreign bodies also cause acute dyspnoea. The former is characterized by fever, rapid onset, severe dyspnoea, and dysphagia. Sudden dyspnoea is suggestive of a foreign body. In treating laryngismus stridulus the epiglottis should be hooked forward by the finger, the conjunctiva stimulated by the touch, and the nasal mucous membrane with a feather. Inhalations of amyl nitrite are of value. Prophylaxis includes regulation of the gastro-intestinal tract. Liquid extract of grindelia, 10 minims in milk every three hours, is of value. In diphtheritic forms tracheotomy or intubation should not be delayed. The tube should be taken out early—about the second or fourth day. Calomel and iron are of value. Non-diphtheritic forms should have the same treatment, as the diagnosis is often uncertain.

OBSTETRICS.

UNDER THE CHARGE OF

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The Induction of Labor.—LITTLE (*Jour. Obst. and Gyn. British Empire*, September, 1910) reports 46 inductions of labor in 3000 cases of pregnancy. The method employed was the introduction through a bivalve speculum of a medium sized rectal tube through the cervix by a flexible metal director. The average time from the introduction of the bougie to the onset of labor was six and one-half hours; the shortest time about half an hour; the longest about twenty-four hours. Twice the membranes ruptured prematurely, but at the onset of labor, and not

as a result of the introduction of the bougie. In 2 cases there was slight hemorrhage after the introduction of the bougie, but in no case was this alarming, as it was easily controlled. A general anesthetic was given in but 3 of the 46 cases. The indications were: Toxemia, 14; disproportion between head and pelvis, 8; protracted pregnancy, 8; tuberculosis, 3; pyelitis, 2; cardiac lesions, 2; foetal death, 2; syphilis, 2; typhoid fever, 2; diabetes, 1; fever during labor, 1; and persistent vomiting, 1. In half the cases spontaneous labor occurred, and in the other half it was necessary to perform some obstetric operation to complete labor. These operations were all those of delivery through the vagina by various methods. Four of the mothers so treated died; in 1 case of persistent vomiting a small quantity of chloroform was given during delivery, and at autopsy extensive necrosis of the liver was found. A second case of severe toxemia had eclampsia after the bougie had been inserted and pains had started. The patient died on the third day, and autopsy showed thrombosis of the cerebral veins with necrosis in the uterine wall. One other patient died with marked œdema of the lungs, and one from general anasarca with chronic nephritis. Excluding those who had fever before the induction of labor—3 in number—in 43 cases there were 6 patients whose temperature rose above 100.6°. There were 19 foetal deaths in the 46 cases; in the 8 cases of contracted pelvis 2 children were born dead and 4 died at term; in 8 cases of protracted pregnancy 1 child died of intracranial hemorrhage. It is interesting to note that the induction of labor was performed for some conditions which are not accepted by all operators as valid indications. The experience of some indicate that syphilis and typhoid fever do not call for the induction of labor. In disproportion between mother and child the foetal mortality was higher than that of elective Cesarean section. In protracted pregnancy the same was true. As has been repeatedly shown by others, disproportion between mother and child is not an indication for the induction of labor, if the life of the mother is to be considered of especial value. In heart lesions induction of labor was serviceable, while in tuberculosis the results for the mother were good; 2 cases of pyelitis recovered rapidly after the evacuation of the uterus, although the same result has been observed when labor was not induced; the case of diabetes recovered after the emptying of the uterus. In 54 cases the cervix was forcibly dilated, in 52 by the hand, after Harris' method, and in 2 cases by the Pomeroy bag. There were 5 deaths in this series, 3 from eclampsia, 1 from placenta prævia, and 1 after pubiotomy. In the last case dilatation was done preliminary to the pubiotomy upon a patient with marked contraction of the pelvic outlet. Dilatation was accomplished without injuring the cervix, but in performing version the arms went above the head, and in bringing them down the vagina and cervix were cut through by the passage of the arm over the sharp edge of the severed bone. The patient died of peritonitis. Of the 52 cases operated upon by Harris' method, lacerations of the cervix occurred in 71 per cent. In 30 of the 34 cervixes so lacerated, sutures were taken at once; and in 85 per cent. immediate union followed; in 6 cases in which union did not occur the ultimate result was not worse than is often seen in spontaneous labor; in the 2 cases in which the Pomeroy bag was used the cervix was torn, but was immediately sutured; 2 of the patients in whom the

cervix was immediately closed had been delivered for the second time, and the course of labor was normal and lacerations of the cervix did not occur. In placenta prævia the danger seems to lie in thrombosis. A normal puerperal period was more frequent after the application of forceps than after version. So far as the child was concerned, when dilatation was performed rapidly, and the mother was in good condition, if the head was not securely engaged, version gave much the better result. In commenting upon the series, the author believes that the method used for the induction of labor has proved more satisfactory than any of the other means suggested for the purpose. Harris' method of dilatation is satisfactory when the application of the forceps must be preceded by the obliteration of the last rim of the cervix. Its dangers are obvious in cases in which the cervix is unusually vascular. The use of the dilating bag is limited to cases in which there is no objection to rupturing the membranes. The bag displaces the head, if already in the pelvis, and anyone who has tried to insert a bag into a cervix admitting but two or three fingers will appreciate the inadvisability of recommending its use in general practice. The necessity for emergency measures in obstetrics, the author thinks, varies inversely with the care given to the patient during pregnancy. Many complications of labor can be anticipated and avoided by the timely induction of labor. Pelvic contraction is not to be considered as an indication for the induction of labor. Prolongation of pregnancy, on the other hand, is more frequently an indication. The passage of the bougie and the introduction of the gauze pack will usually bring on pains within a few hours. Labor may be spontaneous or may be terminated artificially. When the cervical canal is obliterated, its dilatation by the hand is usually easy, and with care reasonably safe. Hemorrhage and infection can be avoided; lacerations of the cervix will frequently occur, and such lacerations should be immediately repaired. This method can be employed without assistance other than the anesthetizer and a trained nurse. It is simple, applicable to many cases; the force used is limited to the fingers of one hand, and the fingers can recognize and estimate the resistance to be overcome.

Ovarian Pregnancy with Diffuse Intraperitoneal Hemorrhage.—LEA (*Brit. Med. Jour.*, October 22, 1910) reports the case of a patient, aged twenty-nine years, married two years. She was suddenly seized with intense abdominal pain, vomiting, and faintness. When seen the pulse was barely perceptible, the abdomen distended below the umbilicus, and very sensitive. Tenderness was more marked in the left iliac region. There was dulness in the flanks and a suggestion of fluid in the abdomen. Menstruation had occurred normally three weeks previously, and there was no hemorrhage from the uterus. On vaginal examination, there was distinct fulness with slight resistance in Douglas' pouch, but no obvious swelling of the appendages could be recognized. On opening the abdomen a large quantity of blood and clots was found free in the peritoneal cavity. The left ovary was enlarged and from its surface projected a thin-walled blood cyst which had ruptured. The right tube was healthy. The blood and clots were removed as completely as possible and the abdomen closed without drainage. With saline transfusion the patient recovered. On examination, a portion of the ovarian cortex was found to have expanded to form the wall of the cyst, and

was continuous with a mass, which, microscopically, showed contained chorionic villi. Sections of the ovary revealed great dilatation of the bloodvessels with areas of hemorrhage, and in one portion a thick layer of lutein cells. Pregnancy probably occurred in a Graafian follicle, the ovarian tissue becoming thinned, forming a capsule for the cyst, and hemorrhage occurred after rupture.

The Origin and Prevention of Puerperal Fever.—At the last meeting of the British Medical Association, DÖDERLEIN (*Brit. Med. Jour.*, October 22, 1910) drew attention to the danger of infection from within the female generative organs themselves, and also the danger of inoculation by pathogenic organisms from without, during labor or the puerperal period. To determine the value of preliminary disinfection of the vagina during pregnancy, Döderlein calls attention to the results obtained in the Tübingen clinic, in which 500 parturient women were treated by irrigation with one quart of solution of sublimate 1 to 1000. During the irrigation the walls of the vagina were rubbed with two fingers of the gloved hand carefully and cautiously, but as thoroughly as possible. All internal examinations were made exclusively with the gloved hand, and the external genitalia were previously disinfected, so that the introduction of microbes from without was excluded. In the same period there were 500 lying-in women who were not subjected to vaginal disinfection. Of the 500 disinfected patients, 12.8 per cent. had fever, while of the 500 not disinfected, 8 per cent. had fever. After deducting those who had fever not originating from the genital organs, there remained 5.2 per cent. with fever among the non-disinfected and 10 per cent. among the disinfected. In the Munich clinic, irrigation was made with from $\frac{1}{2}$ to 1 per cent. solution of lactic acid. The result showed that in 480 parturient women disinfected by this method, 6.29 per cent. had fever, while in 477 not irrigated, only 3.3 per cent. had fever. Similar results in the hands of other observers emphasized the fact that preliminary disinfection during pregnancy should not be practiced in normal parturient women. Döderlein calls attention to a glove which he has devised for use by students and midwives, which facilitates the use of gloves and prevents infection. The glove has but two fingers, the remainder protecting the hands by a mitten. These gloves are cheaper than the usual sort, are disinfected at the factory by steaming, and then packed in a triple cover, impervious to air and bacteria.

The Treatment of Rupture of the Uterus.—MUNRO KERR (*Brit. Med. Jour.*, October 22, 1910) adds 3 additional cases to his previous report of 14. Of the last 3, 2 were treated by hysterectomy and drainage, and 1 was treated—as the tear was incomplete—by gauze packing through the vagina. This patient died five hours afterward. Kerr has performed hysterectomy 11 times, with 5 recoveries. Out of 6 fatal cases, 4 died from sepsis and 2 from shock. He believes that sepsis is the cause of death in these cases, and in his later experience he has completely removed the uterus and drained the lacerated broad ligament by a thick rubber tube brought out through the vagina and loosely surrounded with gauze. The lower part of the pelvis is completely covered with peritoneum. The drain is left three or four days, and the results have been satisfactory.

GYNECOLOGY.

UNDER THE CHARGE OF

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The Present Status of the Colon Tube.—By means of skiagrams, YATES (*Amer. Jour. Obst.*, 1910, lxii, 761) has demonstrated that seldom, if ever, are soft rubber tubes admitted into the normal colon. When an endeavor is made to force the tube upward, even by the gentlest manipulations, it is found to coil itself up in the rectum and there do positive harm because of pressure, irritation, and the consequent inability to retain the encma. In perhaps half the instances it is impossible to tell when the tube is coiling upon itself, even when we suspect it. Colon tubes as such are of no value, because they do not reach the colon, and they are mischievous in that proportion as we endeavor to force them higher up. Water or fluid injected 4 or 5 inches into the rectum is carried upward into the colon, and may be found at the cecum in ten minutes. There is good reason to believe that a reversed peristalsis is set up when fluids are injected into the rectum. The introduction of a tube more than 5 inches for colonic irrigation or other purposes is useless, and likely to defeat the object desired.

Lymphangiectases in Myoma Uteri.—TODYO (*Archiv f. Gynäkologie*, 1910, xci, 641) has made a study of three cases of myoma uteri, associated with marked dilatation of the lymph vessels in the broad ligaments. He was unable to distinguish any evidences of newly formed vessels, and is of the opinion, therefore, that these dilatations are true lymphangiectases rather than lymphangiomas. The production of these dilatations could not be explained on the ground of stasis resulting from occlusion of the efferent lymph vessels by thrombosis, inflammatory alterations, or pressure from without. He could demonstrate no impairment of the vessel walls which would permit of their primary dilatation, and does not accept the theory that an undue supply of lymph leads to their distention. Since his examinations failed to reveal a mechanical cause for its production, he advances the idea that the lymphangiectasis is due to changes in the vessel walls resulting from altered metabolism or intoxication associated with myomas, comparable to those changes observed in the heart and bloodvessels.

The Function of the Corpus Luteum.—From an exhaustive experimental research, FRAENKEL (*Archiv f. Gynäkologie*, 1910, xci, 705) substantiates the theory which he advanced seven years ago, that the corpus luteum is a gland with an internal secretion which brings about the alterations essential to the embedding and early development of the fecundated ovum. Further, the corpus luteum is responsible for the cyclic engorgement preceding menstruation. Examination of the ovaries during the course of operation shows that the follicle ruptures about nineteen days after the beginning of the last menstruation;

about eight days later the yellow body has reached the height of its development, the onset of the new menstruation marks the beginning of its involution, and by the end of menstruation it has disappeared. The administration of corpus luteum extract as a therapeutic measure was of no avail in dysmennorrhœa, irregular periods, and the intoxications of pregnancy; he has had good results, however, from its use in those cases presenting symptoms of vasomotor origin, due to absent or diminished ovarian function. The article embraces an excellent summary of the recent contributions to this subject.

Chronic Intestinal Stasis.—LANE (*Surg., Gyn., and Obstet.*, 1910, xi, 495) defines intestinal stasis as a delay of the contents of the intestine in some portion of the gastro-intestinal tract, but more particularly in the large bowel, which allows of the absorption into the circulation of a larger quantity of toxic material than can be dealt with effectually. This delay is of mechanical origin, due to alterations resulting from pressure, strain, and the development of accessory peritoneal bands, evolutionary in nature, incident to the erect posture. These bands, while, on the whole, beneficial, may become vicious in their action by producing angulations and kinks. Abnormal fixation or kinking of the pylorus may result from bands extending to the liver or transverse colon; deformity of the ileum may result from the contraction of a band which develops on the under surface of the mesentery of the terminal portion of the small intestine. Strong bands of peritoneum are found between the cecum, ascending colon, and adjacent abdominal wall; also at the hepatic and splenic flexures, the angulations thus produced being exaggerated by the weight of the transverse colon. Bands are commonly observed on the outer surface of the mesosigmoid, converting the sigmoid into a straight fixed tube of diminished calibre and atrophic walls because of this fixation. The rectum may be enormously elongated and loosely attached, causing obstinate constipation. Intestinal stasis permits the ascent of deleterious organisms in the small intestine, with occasional infection of the biliary and pancreatic ducts. Constipation is due, chiefly, to a stasis in the large bowel; there may be evidences of a very marked auto-intoxication in cases in which there is a daily evacuation. The symptoms of auto-intoxication are loss of fat, cold, clammy extremities, inhibition of respiratory function, pigmentation of the skin, pain and weakness in the muscles, especially in the legs, arms, and back, and headache. The breasts undergo very definite changes; the upper and outer zone of the left breast becomes hard and nodular, and later the process is manifest in the corresponding zone of the right breast. The process gradually extends to the whole gland in which cysts develop. In the author's experience, brilliant results have attended ileosigmoidostomy or excision of the colon.

The Treatment of Tubal Pregnancy during the Early Months.—FEHLING (*Archiv f. Gyn.*, 1910, xcii, 3) advocates immediate operation in all cases of tubal rupture, as well as hematocele, and condemns postponement in the hope of reaction from collapse. The operation should be performed in a hospital, since the poor facilities of a private house promote delay, and the chances of infection are greater. The abdominal route is preferred in all cases because it affords a better view of the

field of operation, permitting greater rapidity combined with a better opportunity for the examination of the opposite side, which he regards as of great importance. The mere evacuation of a hematocele by the vaginal route is not sufficient, since the diseased tube is left behind to cause further trouble; infection is more likely to occur and convalescence is delayed. Only in the presence of suppuration of the hematocele, or when the test puncture demonstrates organisms, does he resort to evacuation by the vaginal route. Following these radical principles, 170 cases have been operated upon in the Strassburg clinic during the last nine years. Of this number, there were 43 ruptures with free hemorrhage, 3 ruptures with hematocele, 7 ruptures with sacculation of the bleeding, and 93 tubal abortions with hematocele. The remaining 24 cases were made up of simple unruptured pregnancy, tubal abortion without hematocele, etc.; 64 per cent. of the ruptures were found in the isthmus or interstitial (3 cases) portion of the tube; 86.8 per cent. of the tubal abortions resulted from pregnancy in the ampulla. Rupture occurred in 78.5 per cent. of the cases of pregnancies located in the isthmus and 21.4 per cent. of those in the ampulla. All cases of tubal abortion were successfully operated upon; 7 deaths followed operation in tubal rupture. Of the 170 cases, only 22 were nullipara; in 143 cases, 52 per cent. presented disease of the opposite tube or ovary. Fehling believes that in the majority of cases a bilateral tubal disease is the underlying factor in the development of extra-uterine pregnancy. The condition is relatively rare in the better class of women. The rupture is undoubtedly due to alterations produced in the tubal wall by the growing villi; why extensive hemorrhage should occur from such a small opening is more difficult to explain, and he conceives the idea that some substances are liberated at the time of rupture which retard coagulation. An accurate diagnosis can be made in 95 per cent. of the cases; while the onset may be sudden and violent, the history is usually that of a beginning and delayed abortion; the demonstration of a mass behind or to the side of the uterus makes the case clear. Pyosalpinx may simulate tubal pregnancy so closely as to make the diagnosis impossible.

Adenocarcinoma of the Kidney.—SHERRILL (*Amer. Jour. Obstet.*, 1910, lxii, 997) details the histories of 7 cases collected from the literature and reports a case of adenocarcinoma of the kidney which he has successfully operated upon. Primary malignant disease of the kidney is usually unilateral. It may spread by direct invasion of the venous channels, by extension into contiguous tissue, by transplantation metastases into the bladder, and by the lymphatics. Lymphatic metastases occur late in the disease and are comparatively rare. Renal carcinoma appears most frequently between the ages of forty to sixty, although it may occur much earlier, even in foetal life. It is probable that a large proportion of these tumors are of congenital origin, developing from cell rests. While a calculus may favor the development of the growth, it cannot be considered as a direct cause. Hematuria, pain, or the presence of a tumor will direct attention to the kidney. While the prognosis is always grave, radical removal in its early stages will offer about as large a percentage of recoveries as carcinoma in any other portion of the body.

OTOLOGY.

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

The Otitis of Ozena.—LANNOIS and JACOD (*Annales des maladies de l'oreille*, October, 1910) direct attention to the frequencies of middle-ear disease as a complication, or sequence, of atrophic rhinitis and to the similarity of the evidences of the affection in the cases of suppurative middle-ear disease. With reference to the frequency of the aural sequence authorities differ, more recent observers contributing the larger percentages—Michel in 1876, Loewenberg in 1885, and Jurasz in 1891, reporting but few cases; the latter writer finding but 12 cases of aural complication in 170 cases of ozena. Zaufall, on the other hand, estimates the aural sequence of atrophic rhinitis at 80 per cent., and Morf at 47.5 per cent., including aural lesions of various forms. The investigations of the authors substantiate the estimates of Morf, and they have moreover determined a delimitable form of suppurative middle-ear affection occurring during the course of the atrophic rhinitis as a subacute or chronic evolution, its special clinical aspect being presented in the moderate suppurative discharge and the tendency to the formation of brownish or greenish crusts, having the odor distinctive of ozena, and justifying the recognition of the condition, not as a complication but as a true manifestation of the implication of the tympanic mucosa in the corresponding intranasal process, and the differentiative title of ozenous otitis. In the cases of prolonged middle-ear suppuration, with recurrent subacute attacks, there is but little in the objective manifestation or in the way of discomfort to the patient, beyond the impairment of hearing, to direct attention to the aural condition, but there is the peculiar ozenic odor of the purulent aural discharge, and objective examination reveals the resemblances, in the ear, to the condition in the nose, in the moderate amount of purulent discharge, and the firm, adherent, malodorous crusts which often resist removal without preliminary softening. The cases reported support in their history the contention of Lannois and Jacod that they present a distinctive class, the recognition of which is a matter of clinical importance. The local, aural treatment employed is that applicable in nasal ozena, the use of mild mentholated ointment and of hydrogen dioxide, for the softening and removal of the crusts, and the subsequent application of the essential oil of birch, the antiseptic quality of which resembles that of the oil of cade, the medium of application being vaseline, with an admixture of from 15 per cent. to 20 per cent. of the oil of birch.

The Subperiosteal Abscess of the Mastoid Region.—HOLGER MYGIND (*Archiv f. Ohrenheilk.*, 1910, lxxxii, Heft 3, 4) reports 100 observed cases of subperiosteal abscess of the mastoid region, all of which were secondary to suppurative middle-ear disease, there being no case of the

so-called primary subperiosteal abscess. The cases were nearly evenly divided between the two ears and the two sexes, but showed a preponderating frequency in infants and in young children; 15 cases, 12 male and 3 female, were under three years of age; 32 cases, 12 male and 20 female, were between one and four years of age; and 38 cases, 15 male and 23 female, were between the ages of five and fifteen years. The oldest patient was forty-three years of age. As the etiology and pathogenesis of the subperiosteal abscess of the temporal bone is but little mentioned in the literature of the subject, and as this includes matter of much practical importance, a large part of Mygind's paper is devoted to its consideration. In the majority of cases the suppurative tympanic process, which was the origin of the abscess formation, was of the acute type (78 per cent.), 4 cases were of specific origin, 2 originated in scarlatina and 1 in typhoid fever; had the observation included material from contagious wards, the result would have been different, with a preponderating proportion undoubtedly of the cases due to scarlatina; in 3 cases tuberculosis was the primary cause of the preliminary suppurative middle-ear disease. In reference to the lapse of time between the inception of the acute middle-ear suppuration and the sequence of the abscess formation, the records showed that, in 25 cases, this sequence was evidenced within one week, and in an equal number of cases, not until after the lapse of a month, the great majority of the former cases being infants under one year of age. The bacteriological examination of the abscess contents, where this could be made from the pus unmixed with blood, gave streptococcus in the preponderating number of cases (21), and staphylococcus next (8), while in 8 cases in which the pus examined had been admixed with blood from the divided soft tissues, the result was negative; these statistics favored the contention that a staphylococcic angina was commonly the first link in the infective chain. Retention of pus in the tympanic cavity was found to be an etiological factor of importance in reference to the occurrence of the subperiosteal abscess, and, in 15 cases cited, there was no evidence of pus in the external canal and no perforation of the drumhead, while in still other cases the suppurative outflow was small in quantity because of a small perforation of the drumhead or the narrowing of a formerly sufficient outlet by a nipple formation. In 23 cases of a moderate degree of secretion from the middle ear, the pus was malodorous, and this in the acute manifestation, and accompanied by oedema of the posterior, superior, canal wall. In the cases of chronic suppuration the condition of the drumhead made this structure less of an etiological factor in relation to middle-ear retention; but in 16 out of the 22 chronic cases there was cholesteatomatous accumulation in both the middle ear and mastoid, constituting an important factor in the production of the subperiosteal abscess and in the osteitis of the mastoid with extensive and rapid destruction of the bone. In reference to treatment, Mygind's opinion is decided as to the inefficiency of the simple opening of the abscess, by means, for instance, of the familiar Wildes incision, since in all of the reported cases there was not only extensive osteitis, with considerable areas of necrosis, but in many of them those intracranial complications which make for the great fatality of these rapidly progressive cases, even when they come early under treatment, and the proper measure of resection of the mastoid process is applied. In the

majority of the chronic suppurations the bone conditions demanded exenteration, but in very young children the simple mastoid operation sufficed; in these latter cases Mygind re-curetted the granulomatous cavity within a fortnight after operation, allowing the cavity to fill with blood, and closing the opening over the blood clot by means of a secondary suture, the result being, in the majority of cases, effective with a considerable shortening of the after-treatment; when the secondary suture failed, the after-treatment was usually prolonged, averaging from two to three months, both because of the extent of the surgical cavity and the frequent occurrence of intracranial complications. The conclusions of Mygind from a careful and thorough study of his material, are to the following effect: (1) The subperiosteal abscess of the mastoid region is a common otogenous complication occurring especially in infants. (2) The primary middle-ear suppuration is usually of the acute type and the abscess develops, especially in very young children, at an early stage of the middle-ear suppuration. (3) The abscess occurs, almost invariably, as the sequence of an osteitis of the mastoid process; this osteitis is, as a rule, an acute process even when there is an already existant chronic osteitis. (4) When a chronic osteitis of the mastoid exists, it is commonly associated with cholesteatomatous conditions. (5) The osteitis of the mastoid process preliminary to the subperiosteal abscess is usually extensive and frequently accompanied by intracranial complications, implications of the sinus and of its vicinity preponderating. (6) The application of the Wildes incision in these cases is to be strongly discountenanced. The only adequate treatment consists in a mastoidectomy or in a tympanomastoid exenteration.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Pathology of the Conducting System of the Heart.—Low (*Ziegler's Beiträge*, 1910, xlix, 1) has studied the bundle of His and node of Tawara in a large series of hearts at autopsy, with the idea of investigating the frequency with which various common pathological conditions may affect this particular portion of the heart muscle, and whether sudden death in various cardiac diseases might be dependent upon such alterations of the bundle. A total number of 72 hearts were examined, from various acute infectious diseases, nephritis, emphysema, acute ulcerative endocarditis, chronic endocarditis, and myocarditis. In 52 of these cases distinct lesions were found in the bundle; usually the lesion was an acute one, consisting in infiltrations of cells, small abscesses, etc. Occasionally hemorrhages were found, or diseases of the blood-vessels. In a case of acute myelogenic leukemia, a small leukemic infiltration was seen in the bundle. In general, the results accord with

the findings of Monckeberg (*Untersuchungen uber das Otrio-ventrikular bundel in menschlichen Herzen*, 1909), who has studied in a similar manner 70 hearts. In accord with the observations of Monckeberg is the observation that the His bundle does not hypertrophy with hypertrophy of the remainder of the heart muscle. The demonstration that acute lesions are of common occurrence postmortem indicates that terminal alterations in the conducting system of the heart may occasionally be responsible for death in certain instances. With careful study by the phlebogram and electrocardiogram some of these cases may be recognized before death.

Subcutaneous Reaction of Rabbit and Horse Serum.—KNOX and MOSS (*Jour. Exper. Med.*, 1910, xii, 562) have found that anaphylaxis or allergy of rabbits against horse serum can be proved by the subcutaneous test. This is made by the injection of small amounts of horse serum beneath the shaved skin of the abdomen of sensitized rabbits. The specific reaction appears in from twelve to twenty-four hours after the test is made, and reaches its maximum in from twenty-four to thirty-six hours. It consists of a local swelling extending from 0.5 to 2 cm. from the point of inoculation. The skin involved in the raised area is usually red, and hotter than the surrounding skin. The hypersusceptibility sets in usually in from ten to fifteen days after the first injection of horse serum and lasts at least three months, though individual rabbits showed variations from the average time. Almost synchronously with the allergic conditions, precipitins against horse serum appear in the rabbit's blood. No suppression of allergy which would correspond to the so-called antianaphylaxis could be proved, and after large injections of serum the allergic rabbits still reacted subcutaneously. The allergic condition was not transmitted to the young, for the offspring of injected rabbits did not give a positive subcutaneous test. Neither the injection of large amounts of horse serum nor the marked local reaction of the skin produced any variation in the leukocytes greater than may be observed in normal rabbits.

Acute Degeneration of the Liver in Animals with an Eck Fistula Complicated with Pancreas Necrosis.—During some experiments with an Eck fistula in dogs, FISHLER (*Deut. Arch. f. klin. Med.*, 1910, c, 329) found that if the pancreas was injured a train of well defined symptoms developed, ending in death. These symptoms consisted principally in coma, with sensory and motor excitability. At autopsy the most striking pathological changes were extensive central necrosis of the liver, with a few fat necroses about the pancreas. Neither the symptoms nor anatomical changes can be brought about by Eck fistulas alone. On the other hand, extensive injury to the pancreas results in slight changes in the liver, perhaps similar in kind, but not to be compared in extent with those following the combination of an Eck fistula and injury to the pancreas. These liver changes have been noted frequently in pancreas necrosis, and Fischler believes them to be of much importance and caused by the action of the pancreas ferments upon the liver cells. When the blood supply of the liver is interfered with by shunting off the portal circulation into the vena cava, the function of the liver is disturbed and the action of even small amounts of pancreatic ferments is

greatly exaggerated, resulting in the extensive destruction of the lobules, accompanied by coma and death. The clinical feature is not unlike that seen in acute yellow atrophy. Fischler likewise believes that these experiments point to the fact that under normal circumstances the liver possesses an hitherto unrecognized function of destroying ferments. When this power is disturbed the ferments, for instance, of the pancreas, are not dispensed with, and therefore exert their toxic action upon the body. He offers this as an explanation for the death which occurs in extensive pancreatic necrosis.

The Pressor Substance of the Kidneys.—In an earlier communication BINGEL and STRAUSS (*Deut. Arch. f. klin. Med.*, 1909, xcvi, 476) found that it was possible to extract from normal kidneys of various animals a substance which was capable of producing a marked and fairly prolonged rise in blood pressure when injected into rabbits and dogs. This substance had been studied further by BINGEL and CLAUS (*Deut. Arch. f. klin. Med.*, 1910, c, 412). They find that this rise of blood pressure is probably brought about by a contraction of the peripheral vessels. Intravenous injections of rennin preparations were made in rabbits with oncometers placed upon the kidney and extremity. The injection of rennin was accompanied by a marked increase in the volume of the kidney, accompanied by diuresis and constriction of the vessels of the legs, which went hand in hand with the rise of blood pressure. This result is entirely different from that following the injection of adrenalin, which causes a great decrease in the volume of the kidney, an immediate decrease in the volume of the extremity, followed by an increase in the volume caused probably through the fact that blood is forced into the contracted vessels of the limbs through the high blood pressure. Finally, the limb decreases in volume again and the vessels remain contracted for some period of time. The action of rennin was then tried upon animals with experimentally induced nephritis. Sublimate was used for this purpose. Both the kidney volume and blood pressure of these nephritic animals reacted in exactly the same way as they did in normal animals. Finally, an extract of kidney from rabbits suffering from sublimate nephritis was compared with rennin from normal rabbits' kidneys. The extract of these kidneys, which were the seat of sublimate nephritis, gave rise to an entirely different reaction in the normal rabbit. Injections of the pressed juice of the kidney caused little or no effect upon the blood pressure and produced a marked decrease in the kidney volume. Since control experiments showed that this was not due to the presence of sublimate in the kidneys, the authors conclude that in sublimate nephritis the kidneys contain some substance which alters profoundly the normal action of kidney extract.

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All communications should be addressed to—

DR. A. O. J. KELLY, 1911 Pine Street, Philadelphia, U. S. A.

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Obituary


IT is with profound regret that we announce the unexpected death of Aloysius O. J. Kelly, A.B., A.M., M.D., Editor of THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES. For nearly five years he had executed with signal ability and success all the duties involved in the editorial management of the oldest medical periodical in the English language. His preparation for this work was singularly complete. Born in 1869, he entered the Medical Department of the University of Pennsylvania in 1888, graduating in 1891, with a highly creditable record. He then became resident at St. Agnes' Hospital in Philadelphia, where he attracted attention by his unusual knowledge of internal medicine and his resourcefulness in treatment. Thence he went to London, Dublin and Vienna for further study. In the last named city he was easily the leader among American post-graduate medical students, and it is said that he became as well known there as in Philadelphia. With characteristic warm-heartedness he freely gave of his experience to aid those who came later. Returning to Philadelphia he rapidly made his way to the front, becoming Physician to St. Agnes' Hospital, Pathologist to the German Hospital, and rising from the position of Instructor to that of Assistant Professor of Clinical Medicine in the University of Pennsylvania. To those who knew him it was evident that this was but a station on the road of future advancement. During the past year he had delivered the didactic lectures on practice, a duty usually reserved for the head of the department. These lectures were brilliantly successful. For many years he was Professor of Medicine in the University of Vermont, and his improvements in the methods of teaching gave this institution an enviable position in New England. He was also Professor of Pathology in the Woman's Medical College of Pennsylvania. His literary work is extensive and important. Besides numerous contributions in periodicals, all of which are characterized by intellectual grasp and scholarly form, he recently completed a full Text-book on Practice, which is recognized as the best in many respects

that has yet appeared, and he wrote the article on Diseases of the Liver in Osler's *Modern Medicine*. In collaboration with Professor John H. Musser he had partly issued a composite work on *Treatment* in three volumes by many authors.

Dr. Kelly recognized the importance of keeping in touch with the members of his profession, and in turn his own value to his colleagues was appreciated and shown in his election to many distinguished bodies. He was an active member of the College of Physicians of Philadelphia, the Association of American Physicians, the Congress of American Physicians and Surgeons, the County and State Medical Societies, the American Medical Association, the Interurban Clinical Club, the Pathological, Pediatric and Neurological Societies. All these he served faithfully, and in several instances as their presiding officer.

Of Dr. Kelly's character it may be said that he was a loyal and lovable friend, fearless in doing what he considered right and in combating wrong. His personality was one of warmth and singular attractiveness, and his kindly nature won him the affection of all with whom he came into contact. Of pleasing address and fluent as a speaker, he was withal a man of great modesty, one whose worth always remained for others to appreciate. His capacity for organizing and executing work was enormous, and the amount he accomplished seems incredible. His untimely death, coming just at the full development of his remarkable powers, is a great loss to the profession of which he was so eminent a member. To those of his colleagues who had the privilege of knowing him intimately the burden of grief is beyond expression.

PHILADELPHIA, February 23, 1911.



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ORIGINAL ARTICLES.

ON THE PRESENCE OF A VENOUS HUM IN THE EPIGASTRIUM
IN CIRRHOSIS OF THE LIVER.

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X., a physician, aged forty-nine years, had been for years a country practitioner, and had led a regular and exceedingly active life. He had lived fairly well and had taken, probably, three or four drinks of whiskey a day throughout his life. Two years previously he had had an attack of hematemesis, which followed a rather heavy supper. Since that time he had been well until eleven days before consulting me, when, one morning, while driving, he became unaccountably "nervous," coughed and vomited about an ounce of dark blood. Returning home, he went to bed. The vomiting continued, containing as much as a pint and a half of blood. This was followed by repeated tarry stools. He complained also of abdominal pain in the right side of rather an indefinite character. After this attack he placed himself on a very limited diet, but, with remarkable energy, he kept at work attending to a large general practice.

In the consulting room, on November 3, 1905, he was extremely blanched. The pulse was about 100, regular, rather soft. The apex impulse of the heart was in the fourth space within the mammillary line; a blowing systolic murmur was heard all over the cardiac area. The abdomen was full. The border of the liver was palpable one or two fingers' breadth below the costal margin in the mammillary line, and about half-way between the xyphoid cartilage and the umbilicus in the median line; it was smooth and hard. The spleen was readily palpable, descending two or three fingers' breadth

below the costal margin on inspiration. There was no ascites. The hemoglobin, by the Tallqvist scale, was between 20 and 30 per cent.

The patient was advised to enter the hospital, which he did on the following day (November 4, 1905). On entry, he was very pale. Dr. Cole noted that the veins in the epigastrium and along the costal margin were a little distended and that the abdomen was decidedly full, showing a few large veins in the groins and flanks; none about the umbilicus. There was slight dulness in the right flank. The edge of the liver was well felt, smooth and rounded, and the splenic border was 3 cm. below the costal margin in the right parasternal line, reaching forward to within 2 cm. of the median line.

The patient was put to bed and given two Bland's pills (gr. v) three times a day. Improvement was steady.

November 9. Hemoglobin, 33 per cent. (Dare).

November 16. Red corpuscles, 3,400,000; colorless corpuscles, 4000; hemoglobin, 48 per cent.

November 20. Hemoglobin, 56 per cent. The soft systolic murmur over the heart had completely disappeared. The abdomen was symmetrical; the hepatic border was palpable fully two fingers' breadth below the tip of the xyphoid cartilage. *About opposite the sixth costal cartilage, over the lower sternum, just at the base of the xyphoid, there was heard a loud continuous venous hum with slight inspiratory accentuation. It was lost immediately as one passed upward. It was transmitted a little downward, disappearing, however, before the tip of the ensiform cartilage. It was heard about 4 cm. to the right, and, faintly, about 6 cm. to the left.* A few rather large veins were visible at this point, but nothing was felt. "It seems evidently superficial, is entirely absent in the precordial region, left or right. It must be produced by some abnormality of the internal mammary veins." The spleen was still palpable two fingers' breadth below the costal margin.

November 27. Hemoglobin, 75 per cent. The urine throughout showed a very faint trace of sugar, only once estimable (0.4 per cent.) by the polarimeter. On entrance, there was fever, reaching 102° to 103° at night, with morning remissions. After the first forty-eight hours it was below 101°, and during the last week it never reached 100°.

The patient left the hospital on November 27, and returned to his work on Christmas Day.

In January, again, he vomited about a tablespoonful of blood, and noticed several tarry stools. There was fever in the afternoons (99° to 103°), anorexia, and dyspnoea on exertion.

He consulted me on January 19, 1906; in the morning he had vomited a tablespoonful of blood. At this time he was still pale, although the general nourishment was good. The heart sounds were clear, excepting a slight reduplication of the first sound at

both apex and tricuspid areas. At the base, the second aortic was accentuated. The abdomen was full. The liver was easily felt, 7.5 cm. below the tip of the ensiform cartilage. It did not feel quite so hard as on the previous examination. *A loud venous hum was audible in the xyphoid notch.* The spleen descended 8 cm. below the costal margin.

On April 27, 1906 I saw the patient again. Since December he had had three periods during which the stools were tarry. Four or five weeks before he had had a sharp attack of pain in the lower abdomen, followed by the vomiting of about a gill of blood. He was anemic, dyspnoëic, and said he was unable to walk because of dyspnoea and a sense of pain in the precordium. There had been increasing oedema of the legs. He was still very pale. The cardiac apex impulse was palpable in the fifth space, 11 cm. from the mid-sternal line. There was a presystolic gallop and a very slight systolic murmur which was heard about to the anterior axillary line, where it was lost. The murmur was loud and rather scratchy in the pulmonic area, feebler in the aortic, though louder here and over the manubrium than at the apex. There were fine rales at both bases.

The abdomen was a little full; the spleen readily palpable, 7.5 cm. from the costal margin. The liver was easily felt. It did not seem quite so hard, extending only 6.8 cm. below the tip of the ensiform cartilage, 12 cm. above the mid-umbilicus. In the epigastrium, just over the xyphoid cartilage, and a little toward the left *there was felt a distinct, fine thrill. The same loud venous hum was audible.*

The patient gave up his practice temporarily and took a long vacation. On his return he gave up the heavier part of his work, and in the course of a few months recovered his usual health. For four years he was in remarkably good condition and led an active life.

At the author's request the patient called upon him again on October 7, 1910. He was then in excellent general condition. There had been occasional dark colored stools. No more hematemesis. For two and a half years he had had a slight umbilical hernia. He had moved from the country to the city, and given up his practice, but had been active in several responsible positions. There had been in the last several months considerable frequency of micturition and some thirst. He looked remarkably well but somewhat thinner than he used to be; of good color. Hemoglobin (Tallqvist), 85 to 90 per cent. The face was ruddy, the venules on the cheeks and nose dilated. The pulse was slow and regular; the pressure, by estimate, 130 to 140. Nothing remarkable was to be detected in the heart or lungs. The abdomen was rather full; everywhere tympanitic. The liver was to be felt just at the costal margin in the mammillary line; the border was 7.3 cm. from the tip of the xyphoid, 11 cm. from the mid-umbilicus. The spleen was just to be felt a trifle below the costal margin, descending

markedly with inspiration. No thrill was felt at the episternal notch. There was no dilatation of the cutaneous veins excepting the corona hepatica. There was a distinct umbilical hernia, most marked just above the umbilicus. *Just over the xyphoid, not heard below its tip or to the right, but distinctly audible for a distance of about 3 cm. to the left, there was heard the echoing, venous hum before described. It was loudest immediately over and to the left of the xyphoid; was a continuous echoing sound exactly like the bruit de diable in the neck. There was a very distinct inspiratory accentuation. With complete expiration, when the breath was held, the murmur was diminished, and it almost disappeared when the breath was held with complete inspiration. There were no definite changes in connection with the cardiac rhythm.*

No murmurs were heard in the region of the umbilicus; no murmurs over the spleen or in Traube's space. "Such a murmur must be due to the entrance of blood from a smaller into a larger cavity; its situation suggests the point of entrance of Braune's parumbilical xyphoid vein into the roots of the internal mammary."

On Sunday, October 16, 1910, the patient was seized with a sudden attack of nausea similar, his family tell me, to several attacks which he had had during the preceding year, but which he had not mentioned to the author. During the night the vomiting continued, and the patient became drowsy.

On the morning of the 17th he became wholly unconscious. The patient was seen at this time in consultation with Dr. Chambers. He was lying on his back, breathing quietly. The pulse was regular about 80. There was no suggestion of the air-hunger of a diabetic coma. The pupils were equal and of medium size, responding to light. The conjunctival reflexes were not wholly obliterated.

The abdomen was full, bulging somewhat in the flanks. There was well marked dulness in both flanks and everywhere in the dependent parts of the abdomen. This dulness was clearly movable with change of position. The liver dulness was diminished. The border was not palpable, and in the median line the liver could be felt just below the tip of the xyphoid cartilage. The dulness in the mammillary line did not reach the costal margin. The spleen was of about the same size as at the last note. *The venous hum in the epigastrium had entirely disappeared.*

The urine, examined by Dr. Chambers the day before, was free from albumin and sugar, and showed no reaction for bile.

The coma deepened as the day wore on, the respiration and pulse becoming more accelerated. In the evening several violent convulsions occurred, and the patient died at about 10 o'clock at night. A necropsy was not permitted.

In summary, then, in a man, aged forty-nine years, with evidences of hepatic cirrhosis—habits, hematemesis, melena, large, firm liver,

splenomegaly, and a slight glycosuria—there was detected a *continuous thrill and a long, loud bruit de diable in the epigastrium*. The thrill was felt just in the xyphoid region and a little toward the left, above the lower margin of the liver. The murmur, a characteristic venous hum with inspiratory accentuation, was audible in a limited area immediately about the xyphoid cartilage. It was not audible about the umbilicus. There were no cutaneous varicosities. Five years after the detection of the murmur the patient, who, a week before, had been in good condition, was seized with nausea, vomiting, drowsiness, and finally coma, and died in convulsions about thirty-six hours after the onset of his illness. During the last day of his life there was well marked ascites and the epigastric murmur had entirely disappeared for the first time since its detection.

The condition was obviously a portal cirrhosis of the liver in which ascites was absent during the greater part of the course, owing, undoubtedly, to the existence of a free anastomotic circulation. The manner of death was such as is characteristic of hepatic insufficiency.

The remarkable feature of the case, that which throughout was of especial interest to the author, was the presence of the thrill and venous hum in the epigastrium. What was the cause of this phenomenon? There are various possibilities. It might have been a murmur arising in the vena cava inferior and heard loudest in the epigastrium near the point of entrance of the vena cava into the right auricle. Gambarati advances a like hypothesis to account for a murmur which was in some respects similar to that heard in our case.

Piazza Martini (1894) has described a slight soft murmur heard over the hepatic area, especially in the right axilla, which he believes to be due to constrictions in the vena cava as it passes behind the liver, owing to changes in the position or deformity of the latter organ or to pressure from without (tumors, etc.). Pressure or traction on the superior cava from an old pleurisy or pericarditis would seem to be out of the question from the history of the patient and the physical examination. One might, indeed, fancy that, in the course of the cava through the sulcus in the posterior surface of a deformed, cirrhotic liver, constrictions might arise sufficient to result in fluid veins capable of producing an audible murmur.

Several considerations, however, would appear to militate against this hypothesis: (a) The limited area in which the murmur was heard. A murmur of such intensity arising in the inferior cava behind the liver should be audible over a considerably larger area, as it was, indeed, in Gambarati's case. (b) It is hardly conceivable that a murmur arising in the inferior cava should cause a distinct epigastric thrill. (c) The murmur was audible with greater intensity on the left side of the epigastrium, and the thrill was detected only on the left, that is, at a point not over the superior cava.

Might the murmur have arisen in dilated coronary veins or in œsophageal hemorrhoids which, in view of the hematemesis, were in all probability present? The situation in which it was heard might, indeed, support the former hypothesis. That a palpable thrill could be transmitted from veins so deeply placed seems, however, scarcely probable.

The murmur could hardly have arisen in a large umbilical or par-umbilical vein, because of its absence in the neighborhood of the umbilicus or between it and the tip of the xyphoid.

The thrill would suggest that the veins in which the vibrations arose must have been in or in close apposition to the abdominal wall. It seemed to us from the outset probable that these vessels were varicosities dependent on anastomoses between dilated venules in the suspensory ligament and radicles of the internal mammary veins. The immediate cause of such a murmur would appear to be the passage of blood under considerable pressure from a smaller into a larger vessel, or, indeed, the passage of blood through a single vessel with varicose dilatations.

On turning to the literature one finds a considerable number of contributions on the subject of venous murmurs in the epigastrium.

Pégot, in 1833, described an instance of cirrhosis of the liver with great dilatation of what he regarded as a persisting umbilical vein, attended by remarkable varicosities about the umbilicus and in the epigastrium. Over these veins one could hear a slight murmur—"par l'auscultation, on entendait un léger bruissement qui n'était sensible qu'à l'ombilic."

Bamberger, in 1851, reported a similar case with enormous pyramidal varicosities between the umbilicus and ensiform cartilage. With the hand over these veins, a slight thrill was to be felt, and, with the stethoscope, a continuous rustling sound could be heard.

Since this time many observers have referred to the thrill and murmur which may at times be heard over the varicosities occasionally seen about the umbilicus and in the epigastrium in cirrhosis. Charcot, indeed, says: "A murmur which one hears by auscultation, a thrill which the hand detects, are perceived over these veins. They are," he says, "on general principles, signs of a favorable import."

Catti describes a case of cirrhosis with cutaneous varices in the epigastrium, especially of the left vena epigastrica tegumentosa. Over this vein a few centimeters to the left of the navel, an intense thrill and loud murmur were audible—a characteristic venous hum. Below, over the abdomen, there could be heard a musical ringing sound like that of an Æolian harp. By compressing the vein about 1 cm. below the point where the thrill was most marked, the whole phenomenon stopped abruptly, to begin again on removing compression. Pressure above had no effect. At autopsy, the sub-peritoneal veins were found to be large and the ligamentum teres was

voluminous. Such a murmur was clearly due to blood passing under rather a high pressure from smaller anastomotic vessels into the dilated vena epigastrica tegumentosa.

There has been more or less discussion as to the exact nature of the disturbances of circulation causing these extensive varicosities. Rokitsky's original contention that the condition was associated with the dilatation of an incompletely obliterated umbilical vein was disputed by Sappey, who showed that some, and contended that all, of these instances were dependent on dilatation of small parumbilical veins running in the broad ligament. While this is doubtless true in many, perhaps in the majority of instances of extensive *caput medusæ*, the observations of Bamberger, Hoffman, Baumgarten, Picchini, and others show that in some instances at least the large vein in the ligamentum teres is truly a persistent umbilical vein which has been distended as a result of the abnormally high pressure in the portal system.

There are, however, other instances in which a loud venous hum has been audible in the epigastrium in cases of hepatic cirrhosis *without* the presence of notably large cutaneous veins. Sappey, in 1859, describes a case which was demonstrated to him by Trousseau. The patient was a man of about fifty, with cirrhosis of the liver. "On applying the ear or the stethoscope to the abdomen of this patient, one perceived a very distinct bruit, consisting in a sort of continuous murmur." At necropsy, there was found "a voluminous vein extending from the sinus of the portal vein toward the umbilicus, where it ramified and anastomosed with the epigastric veins, which seemed to be its prolongation. Underneath the vein, in the free border of the suspensory ligament, was to be seen the cord of the umbilical vein." Sappey concludes that this large vein was the result of the dilatation of one of the venules which accompany the umbilical vein, and not of the vein itself.

Picchini, in a case of cirrhosis in a boy of sixteen, noted a well-marked thrill on palpation in the epigastrium. This was present in a fairly extensive zone, extending from 1 cm. under the apex of the xyphoid to the umbilicus, with its maximum intensity along the median line, diminishing toward the sides so as not to be felt beyond either parasternal line. It ceased immediately below the umbilicus. It was continuous, slightly diminished by pressure. On auscultation, there was an intense murmur unmodified by respiration or by heart sounds, best audible when the stethoscope was lightly applied, and loudest a little above the umbilicus. The spleen was large; the liver was rather small. There was ascites. After tapping, the murmur became less intense and was limited to the median line. At necropsy, the external anastomoses about the umbilicus were slight. On the internal surface, along the median line, a large single trunk was found, "which, from the umbilicus, along the fold which unites this with the triangular ligament of the liver, had an upward

direction, reached the inferior surface of the liver at the incisure which separates the right from the left lobe, and then folding itself under this, continued toward the hilum of the liver." On further dissection, it was shown that this vein left the anterior surface of the portal vein 3 mm. before its bifurcation at the hilum. Here it was more than one-half as large as the portal. After a course of 2 or 3 mm., it received three trunks of from 2 to 3 mm. in diameter, one after the other, one from the branch of the portal vein destined to the right lobe, the other two from the branch directed to the left lobe. By these additions, the vessel acquired a volume as large as that of the portal vein. In its course along the concave surface of the liver it received no new branches and none between the liver and the umbilicus. There were varicose dilatations about the umbilicus. Picchini considers this a true although somewhat anomalous umbilical vein, firstly because he could find no trace of the obliterated vein, and secondly, because of the absence of anastomoses in its course between the liver and the umbilicus.

Audry mentions the case of an individual, aged fifty years, with exophthalmic goitre, jaundice, and a liver descending to the iliac crest. Above the xyphoid process and along the linea alba there was an intense, continuous souffle, with systolic accentuation, analogous to the murmurs of the chlorotic. Below the umbilicus, a systolic murmur only was heard. No necropsy was reported.

Herbert Davies is quoted by Verstraeten as having described an analogous case. He found a continuous snoring murmur, varying in intensity with inspiration, and occupying the epigastric region to the right of the median line, a little above the umbilicus. This abnormal murmur existed in an individual suffering from hepatic cirrhosis. Davies regarded it as dependent on a collateral current which was established between the portal and epigastric veins.

F. Taylor describes the case of a boy who showed the first evidences of cirrhosis of the liver at six, dying at twenty. He had been ascitic and had had various attacks of hematemesis, but the ascites had disappeared. Death resulted from a general infection. During the year before death an epigastric venous hum was noted. Particulars as to the anastomoses in the epigastrium are not given.

Von Jacksch (1893), in a case of cirrhosis with large liver and spleen, observed a remarkable thrill, which was palpable when the hand was laid on the abdominal wall between the umbilicus and ensiform cartilage. On auscultation in this area one could hear a humming murmur, which might best be compared to the rumbling of a threshing machine. No mention is made of dilated cutaneous veins. At necropsy which revealed a high grade of cirrhosis, "the vena coronaria ventriculi, which opened here 1 cm. above the vena lienalis, into the trunk of the vena portæ, was greatly distended, markedly tortuous, and beset with many varicose dilatations which, in part,

were so large as to admit the extremity of the thumb and to form true blood cysts." The vena umbilicalis was wide open from the left main branch of the portal vein for a space of 7.6 cm., at which point it connected with a thin-walled, varicose Sappey's vein coming from the umbilicus and of an average diameter of 8 mm. From this point to the navel the umbilical vein was pervious only for a hair sound. "From this observation," says von Jacksch, "there can apparently be no doubt that the murmurs which were heard in the case arose in the vena coronaria ventriculi."

Scheele, in a man of forty-six, with jaundice, ascites, and a large, tender, and uneven liver, detected in the region of the umbilicus a very well marked continuous thrill. There was no dilatation of the cutaneous veins. In the dorsal decubitus there was a distinct *bruit de diable*, accentuated on inspiration and diminished on expiration and by pressure on the crural veins. It disappeared in the erect posture, was audible only in the umbilical region, and was not transmitted toward the heart. There was no apparent abnormality in the heart or large veins.

Gambarati, as above mentioned, has described an interesting case which in some respects resembles that described by the author. The patient was a man, aged forty-nine years, with a retracted right chest from an old pleurisy, and an apparent hepatic cirrhosis. The liver was small, the superficial abdominal veins were dilated, especially in the epigastrium passing up toward the chest. The spleen was enlarged. There was ascites. Over the sternum and all over the hepatic area there was a continuous murmur similar in character to the ordinary venous hum in the neck. It was composed of two phases, varying in duration and intensity. The author compared it to the murmur or roaring of a strong wind blowing through a small orifice, and the variations in the intensity of the murmur reminded one of the irregular gusts and lulls of such a wind. Sometimes the murmur appeared more intense with cardiac diastole. It was very superficial and its point of greatest intensity was distinctly at the base of the xyphoid, but it was not heard below or over the xyphoid itself. On very deep, long breaths it seemed louder—clearly a humming-top murmur. It was not altered by lying on one side or another, but was a little louder in the erect posture, and when, after standing, the patient suddenly lay down and assumed the knee-elbow posture, it sometimes diminished or even disappeared for a time. On tying a tight bandage about the chest a few centimeters above the base of the xyphoid, the murmur became weaker, but if the bandage was applied below the costal arch, it became much feebler and sometimes even disappeared. Gambarati believes that the murmur was due to "a constriction of the inferior cava in its passage through the hepatic sulcus, dependent on atropic changes in the liver."

Rolleston says: "In rare instances, a venous hum may be heard over the epigastrium, which is increased on inspiration. It has been explained as the result of compensatory dilatation of the venous communications between the portal and general systemic veins. The thin-walled and dilated veins may readily be kinked as the result of adhesions, or temporarily distorted by the descent of the diaphragm, or even by the pressure of a wooden stethoscope.

"In a man, aged forty-three years, who was under my care at St. George's Hospital, there was a continuous *bruit de diable* in the neck. At autopsy, the liver was markedly cirrhotic and the round ligament contained a thin-walled vein as large as the little finger." This is stated to have been a parumbilical vein.

Catti describes the case of a man, aged fifty-one years, with atrophic cirrhosis and a palpable spleen. The cutaneous abdominal veins were moderately dilated. In the xyphi-sternal notch a very loud venous hum was audible, which was transmitted with diminished intensity as far as the mid-sternum; it was increased on inspiration. There was no thrill. After paracentesis of the abdomen the murmur was much less intense.

It should, however, be remembered that epigastric venous murmurs are heard under other conditions. Roeser, in 1862, comments on the occasional presence of a continuous murmur in the epigastrium in advanced cases of splenic enlargement, apart from the not infrequent soufflé in the splenic artery. Moreover, he says: "There are cases where the portal vein is accessible; it is here a continuous murmur."

Piazza-Martini (1898), in three cases of chronic splenic tumor, has heard a venous hum in Traube's space below the apex of the heart from the sixth space to within 1 cm. of the costal margin, and between the left parasternal and anterior axillary lines. In the right lateral decubitus the area in which the sound was heard was lower down and farther out. When lying on the left side it was heard higher up and nearer the parasternal line. He is inclined to think that it arises in the coronary vein of the stomach.

Von Jacksch describes an instance of cirrhosis in which a venous hum was audible in the left side of the epigastrium in the angle between the large liver and the spleen. At necropsy the splenic vein was found to be so far dilated as to admit the tip of the little finger. All the radicles of the portal vein were dilated, as well as the veins in the lesser omentum and those in the ligamentum teres. "From the anatomical observations there can be no doubt that the murmurs arose in the splenic vein." It must be said that the character of the murmur appears to have been not so distinctly that of a venous hum as in some of the other reported cases.

Catti asserts that in his experience a venous hum is audible over the spleen in nearly every fifth case of chronic tumor; this was best heard, as a rule, over the anterior part.

Other observers have called attention to the occasional presence of a venous hum in the epigastrium just above and to the right of the umbilicus—a hum which is believed to arise in the vena cava inferior.

Cejka, in 1850, says: "With yielding abdominal walls, one needs only to seek the ascending vena cava with the stethoscope according to the dictates of anatomical topography, to perceive a humming murmur (*Nonnengeräusch*) to the right of the median line, and to follow it downward in the course of the vein to the point of its division."

Hammernik, in 1853, describes at length the venous hums over the crurals and inferior cava. These murmurs are usually found only in young and anemic individuals, and may be followed upward from the crurals to the inferior cava. "This venous hum (*Nonnengeräusch*) is continuous, shows no period of accentuation, and is not altered by the respiratory movements."

Friedreich, in 1881, says: "I have myself heard these not infrequently by pressing slowly and continuously on the right, near the linea alba, at about the level of the navel, with a stethoscope with a wide funnel, until the vein in the depths is fully compressed; this is easy to accomplish with the patient on his back and the legs drawn up, especially in those individuals with lax abdominal walls. On suddenly letting up the pressure, there is a loud, rapidly diminishing venous hum. Sometimes, if pressure is properly adjusted, there is a continuous singing or humming murmur." In one case such a murmur disappeared on pressure on one or another crural vein.

Audry asserts that the presence of a venous hum in the epigastrium, a little above and to the right of the umbilicus, is by no means rare. It is similar in character to a diastolic venous souffle, and it is, he thinks, due to the emptying of the veins with diastolic filling of the ventricle. He has not been able to confirm Friedreich's observation of the disappearance of the murmur by pressure on the crural vein. The timbre and the continuous character of the sound, as well as its localization over the vena cava inferior, justify placing this phenomenon among the venous murmurs. Audry comments on the fact that in the several notes on epigastric venous hum in cirrhosis, no mention is made as to the differential diagnosis between it and these murmurs, which he believes due to vibrations arising in the vena cava inferior. He was able to detect these hums in ten out of forty cases. Most of the patients were anemic or suffering from conditions associated often with low blood pressure and vasodilatation, *i. e.*, neurasthenia, typhoid fever, pelvic peritonitis. The murmur which was sometimes audible on pressure, would appear to be similar to that described by Friedreich.

Verstraeten asserts that venous hums in the epigastrium are not very rare. He has been able to make out such murmurs in six out

of 100 cases. They arise, he thinks, at the point where the vena cava enters the liver.

Yet another form of venous hum has been described in the region of the liver. Piazza-Martini (1894) notes a continuous venous hum, which is audible sometimes in the right axilla over the liver. This he regards as entirely different from the epigastric murmur. It is, he believes, due to pressure on the vena cava by a displacement or rotation of the liver or by extrinsic compression or tumors within the vessel. Verstraeten also is familiar with this murmur, which he likens to a distant waterfall. It is accentuated with full inspiration and is audible, especially in marked anemias.

The writer has, in a limited number of cases, sought for the murmur described by Friedreich and others as arising in the *vena cava inferior*. By following Friedreich's technique, it is indeed possible to produce in some cases a slight venous hum. In one very anemic man it was fairly loud. This is, however, quite distinct from the loud murmur and palpable thrill heard in our patient and in the several other cases of hepatic cirrhosis above described, on light application of the stethoscope.

With the soft murmur in the right axilla described by Verstraeten and Piazza-Martini, I am unfamiliar. It is, however, not to be confounded with the epigastric venous hum of cirrhosis.

To return to our own case. The phenomena here observed were somewhat different from most of those reported in the literature. In Audry's first case—a man, aged fifty years, with exophthalmic goitre, jaundice, and a liver descending to the iliac crest—there was a continuous souffle, very intense, with systolic accentuation, analogous, according to the author, to the souffle of the chlorotic. This was heard above from the xyphoid, along the linea alba. Below the umbilicus there was a systolic murmur alone. In this instance the murmur was apparently loud and heard well up to the xyphoid notch, over a liver which may have been cirrhotic. Such a murmur may have been due to varicosities in the abdominal wall or suspensory ligament.

In most of the other cases the position of the murmur was such that it may well have depended on large umbilical or parumbilical veins.

The cases of Gambarati and Catti and one of the cases of von Jacksch are most similar to that which forms the subject of this communication. In all of these instances the point of maximum intensity of the murmur was at the base of the xyphoid process. In von Jacksch's patient, to be sure, the thrill was felt at a point somewhat lower than in our case. In the other two instances, however, the point of greatest intensity of the murmur was at the base of the xyphoid.

In Gambarati's patient the distribution of the murmur was remarkably wide, extending over the entire hepatic area and to the episternal notch. This wide distribution of this murmur might be regarded as supporting his hypothesis that it depended upon fluid veins arising in the inferior cava. Against such an hypothesis, however, would seem to be the complete absence of the murmur in the back. This he accounts for by the statement that there was hydrothorax on the right side. It should be observed, however that he also asserts that the right chest was retracted from an old chronic pleurisy, a condition which it is difficult to harmonize with the presence of a hydrothorax.

Of all the cases in the literature that of Catti is the one which is most analogous to ours, and the hypothesis which he advances to explain the phenomenon agrees entirely with our own conclusions, formed before we were familiar with his communication.

In our patient the limited area of transmission, the extremely superficial character of the murmur, and especially the presence of a thrill, seemed to us, as has been said, to suggest that the murmur arose as a result of anastomoses in the abdominal wall between veins derived from the suspensory ligament of the liver and radicles of the internal mammary vessels. Catti, in his excellent article, refers to the admirable studies of Braune, who, indeed, has described a venous link which connects the large parumbilical vein (Sappey-Luschka) with the left vena epigastrica superior profunda in the neighborhood of the xyphoid. In Braune's own words: "This venous link extends above the fascia transversalis umbilicalis of Richet, from the larger parumbilical vein near the obliterated umbilical vein, passes between the folds of the suspensory ligament of the liver for a certain distance upward behind the sheath of the rectus, breaks through this close by the middle line and, behind the muscle substance of the rectus, in the anterior side of the posterior fold of its sheath, near the xyphoid process, it enters into the left vena epigastrica superior profunda. It is a double, well recognizable and easily injected vessel, which, therefore, leads from the sinus venæ portæ upward to the mammaria interna." Braune further points out that by the transverse xyphoid vein this vein must carry the blood from the portal to the internal mammary of both sides. He regards this vein as a regular structure.

Catti is inclined to consider the murmur in his case, which is so similar to ours, as dependent upon vibrations arising from the passage of blood from Braune's veins into the left deep epigastric vein, the root of the internal mammary. Such an hypothesis would seem to be directly applicable to our case, more so, indeed, than to any other instance in literature.

To what may we ascribe the disappearance of the murmur during the last hours of life? This is, of course, a question which, in the

absence of a necropsy, cannot be answered. The coincidence of the onset of ascites with the disappearance of the murmur might suggest the possibility of thrombosis. The fact, however, that a loud venous hum, sometimes accompanied by a thrill, may be detected in the epigastrium in cirrhosis of the liver, is worthy of emphasis. It is not inconceivable that this phenomenon might, on occasions, prove a point of diagnostic value. It would be well that its occasional occurrence might generally be recognized.

In conclusion, it may be said: (1) A venous hum accompanied sometimes by a well-marked thrill may be detected in the epigastrium in some instances of hepatic cirrhosis.

2. The thrill and murmur may be appreciable: (a) directly over the extensive cutaneous varicosities, or (b) in instances where there is little or no external evidence of venous engorgement.

3. In most of the cases where an epigastric venous hum has been heard in cirrhosis, in the absence of cutaneous varicosities, the sound has been audible best about the umbilicus and along the median line in the epigastrium—in other words, along the course of the round ligament.

4. In a few of these instances it has been found that the incompletely closed umbilical vein has become greatly dilated as a result of increased portal pressure. In others, a large dilated vein has been found in the round ligament running alongside of the obliterated umbilical vessel—doubtless a dilatation of a small parumbilical vein.

5. These murmurs should be distinguished from the slight venous hum sometimes heard in the anemic just above and to the right of the umbilicus, over the inferior vena cava—murmurs which may be brought out by pressure in thin individuals. These murmurs are said to disappear in some cases with pressure on one or another femoral vein (Friedreich).

6. A venous hum has been described in Traube's space and in the left side of the epigastrium in the angle between the large liver and spleen in cirrhosis (von Jacksch, 1899) and in splenic enlargement (Piazza-Martini, 1898), which may arise in a varicose splenic vein.

7. A well-marked thrill and an intense venous hum may be heard in hepatic cirrhosis over a limited area in the epigastric notch, in the immediate neighborhood of the xyphoid cartilage, at a point so far above the lower border of the enlarged liver that it cannot depend upon currents in a varicose umbilical or parumbilical vein. Such murmurs may, in some instances, arise in varicose coronary veins (von Jacksch), while in others, as those observed by Catti and the author, the seat of origin is probably in anastomoses between the roots of the internal mammary and the inferior deep epigastric vessels, very possibly to the entrance into these latter veins of an enlarged parumbilical-xyphoid vein of Braune.

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THE DIAGNOSIS OF DUODENAL ULCER.¹

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WITH increasing experience the conviction is forced upon us that duodenal ulcer is a much more frequent occurrence than we used to think, and that we do not recognize it as often as we should. The physician who graduated fifteen or twenty years ago was taught that ulcer of the duodenum was a rare disease, most often due to external burns. Even ten years ago the teaching was still to the effect that the condition is unusual, not to be compared with gastric ulcer in frequency. But the past decade has gradually changed the views of the profession in this matter; and particularly in the past five years has evidence been forthcoming that duodenal ulcer is more common than gastric, and a possibility always to be reckoned with in the diagnosis of disease in the upper abdomen.

This change of view has been brought about by surgery, demonstrating actual facts to take the place of previous theory. In America, the Mayos, and in England, Moynihan, have conclusively shown by their operative work how frequently duodenal ulcer occurs. Wm. J. Mayo,² reported 272 operations for duodenal ulcer, and his statistics showed that ulcer is more frequent on the duodenal than on the gastric side of the pylorus. Moynihan has recently summarized his previous papers on the subject in a monograph,³ reporting 186 cases, calling attention to the frequency of duodenal ulcer and to the definite clinical picture that it presents. As Mayo says, we are not to assume from all this that duodenal ulcers are more frequent than in the past, but merely that they have heretofore been mistaken for something else. How are we to prevent such mistakes in the future? And how are we to recognize the condition before the surgeon finds it at an operation advised for some other diagnosis?

Recognition of duodenal ulcer depends largely on the *clinical history*; and too much time cannot be spent in carefully working this out in all its details. As a point of beginning, the complaint is of recurring attacks of pain in the upper abdomen, and the important points about which the patient must be questioned are these: The length of time during which these attacks have recurred; their frequency; the patient's condition in the interval; the effect they have had upon nutrition; regarding the attacks themselves, we must inquire the site of pain, its radiation from that site, its

¹ Read at a meeting of the Yolo County Medical Society, Woodland, California, October 4, 1910.

² Jour. Amer. Med. Assoc., August 15, 1908, p. 556.

³ Duodenal Ulcer, W. B. Saunders Co., 1910.

intensity, its character, the time at which it comes on, its duration, what gives relief, what other symptoms accompany it. The story elicited by such a plan of questioning is usually quite characteristic; so characteristic in fact, that Moynihan⁴ says it is diagnostic and justifies operation even without physical examination.

Traced by such a systematic interrogation, the patient's history in duodenal ulcer is that these attacks of pain have recurred for years past, sometimes ten or fifteen, sometimes as far back as he can remember. Of course, it is conceivable that a case may be seen early, after the first or second attack, without such a long-continued history, but usually at the outset the patient makes light of the trouble, attributes it simply to acute indigestion and so postpones seeking advice. The frequency of recurrence is very variable. An attack may come but once a year or once in several months; or for a time attacks may recur every few weeks or even every day, and then there may be no more for many weeks. Patients often give a story of "bad spells," when attacks repeat themselves frequently; then of a varying interval of entire freedom before another recurrence. In the interval between attacks patients with uncomplicated duodenal ulcer usually feel perfectly well, eat what they please, and have no complaint to make. In other cases, however, there is complaint of persistent "acid dyspepsia," burning distress some hours after food (heart burn), regurgitation of mouthfuls of sour water at the height of digestion (water brash), flatulence, and belching. But serious disturbance of digestion, with nausea and vomiting, usually means some complicating condition or some different disease, and is not a part of the ordinary clinical picture. The nutrition does not suffer, and patients with a long-continued history of painful attacks may remain well nourished or even obese. There are exceptions to this rule, but they are due again to complications, or to voluntary reduction of diet by the patient, induced by the fear of attacks.

Coming now to the story of the attacks themselves, the site of pain is the epigastrium, high up toward the ensiform process and near the middle line. From this situation the pain radiates through to the back, to one or the other side of the spine; sometimes it is felt in the back even more severely than in the epigastrium; usually it runs straight through. In character and intensity the pain is severe, but does not compare with that of hepatic or renal colic, nor is it colicky or intermittent like these; patients describe it as aching or dragging or piercing, but in most instances as not unbearable. One of the most characteristic features about the attacks in duodenal ulcer is the time at which the pain occurs with reference to meals; it is several hours, as a rule, three or four at least, after food is taken. Often the attacks come in the night, about mid-

⁴ Duodenal Ulcer, p. 109.

night or at one or two in the morning, waking the patient from sleep. If they come during the day, it is late in the forenoon or afternoon, as the patient grows hungry for the next meal. In duration the attacks are variable, depending upon what is done to relieve them. An hour, or several hours, may pass without relief, the pain coming gradually and going gradually, if left to take its own course. Relief may be obtained in several different ways, which the patient has usually discovered for himself. The most characteristic method is by the taking of food, so that patients learn to have food of some kind at hand, to eat if an attack comes on at night. In other cases, bicarbonate of soda taken freely will afford relief. In still others, drinking freely of water suffices. In all cases, external application of heat is grateful. Associated symptoms are unusual with the pain of uncomplicated duodenal ulcer; there is no nausea, no vomiting, no sweating. Subsequent bad effects are likewise unusual; the epigastrium may be left tender for a day after the attack is over, but the appetite is good, the digestion unimpaired, and the general health as satisfactory as before.

When we turn from this definite and clear-cut picture of the patient's troubles to the *physical examination*, we find a surprising lack of evidence to aid us. In fact, it is this manifest discrepancy between symptoms and physical signs that makes the case suspicious. On inspection of the abdomen there is no abnormality in an uncomplicated case. On palpation, likewise, there is none, unless after a recent attack of pain, when tenderness may be found in the epigastrium or right hypochondrium; but no palpable mass and no succussion splash. Examination of the stomach is negative; there is no evidence of dilatation or of pyloric obstruction. As regards the secretion, the usual finding after a test meal is hyperchlorhydria; in fact, Moynihan⁵ makes the remarkable assertion that "hyperchlorhydria is the medical term for the surgical condition of duodenal ulcer." And in another place he says, "recurrent severe hyperchlorhydria is duodenal ulcer." But on the contrary, hyperacidity may not be found in cases of undoubted duodenal ulcer. In fact, the free HCl may at times be less than the normal amount, and the absence of hyperchlorhydria is not an absolute bar to the diagnosis. Finally, there is but one other item in the laboratory findings to aid us in reaching a conclusion, namely, occult blood in the feces. This is almost invariably present in any active case, with frequently recurring attacks of pain, but may be absent for weeks or months during the intervals of health. The examination of the patient thus adds but little to our knowledge of the case. Yet most clinicians will be unwilling to accept Moynihan's conclusion that "it is, therefore, not necessary to the attaining of an accurate diagnosis that any examination of the patient be made."

⁵ Loc. cit., p. 117.

The following recent case histories show upon what data the diagnosis of duodenal ulcer is considered justifiable:

CASE I.—Mrs. M., aged forty-eight years, first consulted me in August, 1910. She said she had been ailing for the past ten years with recurring attacks of pain in the upper abdomen, coming about once a year. Between these attacks she felt perfectly well. There had been no loss of weight until the past six months, while she was on a special diet. The pain was felt "in the pit of the stomach," ran through to the back, was very severe, as a rule, but the attacks varied in intensity, were cramp-like in character, came on gradually and went away gradually, usually appeared about midnight, never lasted over one or two hours, were relieved by hot applications, but never had required morphine, never were accompanied by nausea or vomiting. In February, 1910, she had a severe attack, after which she was advised to live upon a diet consisting only of vegetables and fruits. Since then, while following this diet, the attacks of pain had come more frequently—once a month or even less. These recent attacks, like all the others, usually came in the night, about midnight, as a rule, rousing her from sleep. In character they were like those described. Between them she had a very good appetite and no distress after food. With none of them and following none of them had she ever been jaundiced. On physical examination, the patient pointed to the epigastrium, just at the lower end of the sternum, as the site of pain. There was no visible or palpable abnormality over the stomach or gall-bladder; no tumor, no succussion splash, no peristaltic wave, no especial rigidity, or tenderness. On inflation of the stomach, the greater curvature was found at the navel. The test meal showed a total acidity of 50, and the free HCl 24. After three days of a meat-free diet, the feces showed a positive reaction for occult blood.

CASE II.—Mrs. C., aged sixty-six years, was first seen in August, 1910. She had had recurring attacks of so-called "acute indigestion" for years past, repeated two or three times a year. In the intervals she felt well, but occasionally belched gas and had eructations of sour fluid. She had not lost in weight. The attacks were characterized by pain in the epigastric region, which frequently radiated through to the back. They usually began three or four hours after eating and most frequently at night, about 1 A.M., rousing her from sleep. She never had vomited with her attacks or felt nauseated, and never had been jaundiced. She had found relief by taking food or bicarbonate of soda. During the past four months the attacks had come more and more frequently, but she generally had several days of good health between. They had also grown more severe, so that recently she had repeatedly required morphine for relief. They always began three to four hours after eating and most often in the night. On physical examination, there was no visible or palpable abnormality in the contour

of the abdomen, no rigidity, no tumor. The greatest tenderness was found in the epigastrium. There was no tenderness over the gall-bladder. On inflation of the stomach the greater curvature was found at the navel. After the Ewald test meal a marked hyperchlorhydria was found, the total acidity being 96, the free HCl 60, and the combined HCl 24. On a meat free diet, the feces repeatedly failed to give any reaction for occult blood. While under observation in the hospital this patient had one of her attacks of pain. It came on late in the evening, several hours after food; was characterized by gradual onset, a sense of distention and fulness in the stomach, sour eructations of a mouthful of fluid, heartburn, belching, but no nausea or vomiting; the pain was in the epigastric region, and gradually grew so severe that morphine had to be given; it ran through to the back, but not to the right costal margin or beneath the right shoulder blade. The next morning the patient had no further pain, but tenderness was found in the epigastrium to the right of the median line about half way between the ensiform and navel; also in the back, just to the right of the tenth dorsal vertebra.

The clinical picture of duodenal ulcer is thus seen to be fairly well defined, but at times it is not so clear as here set down, and when blurring occurs it is because of some complication that has confused the outlines. The complications most frequently seen are: (1) Coincident gastric ulcer; (2) stenosis of the duodenum; (3) hemorrhage; (4) perforation.

1. Though *gastric and duodenal ulcer* may co-exist, fortunately for diagnosis the combination is unusual. Mayo⁶ found that in only 8.2 per cent. of his cases were there separate and distinct ulcers of each organ. Moynihan,⁷ however, in 186 cases operated upon, found both gastric and duodenal ulcer present in 47. The presence of a gastric as well as a duodenal ulcer must necessarily confuse the clinical picture, by producing some of the signs and symptoms of each. It would then become manifestly impossible to make a differential diagnosis between the two. The possibility of the combination is not so remote but that it must be borne in mind in interpreting the clinical findings of any case not conforming to type.

2. *Stenosis of the duodenum* may result in any long-standing case, from fibrosis and cicatricial contraction of the ulcer base. Then the same train of symptoms and signs present themselves as in stenosis at the pylorus due to a gastric ulcer. The clinical picture is one of food stagnation, with regurgitation and vomiting, and of dilated stomach, easily discovered by succussion splash, by retained food in the fasting organ, and by the outline after inflation, and ultimately by definite and often vigorous peristaltic waves

⁶ Jour. Amer. Med. Assoc., loc. cit.

⁷ Monograph on Duodenal Ulcer.

across the stomach wall. When such a complication arises, it is impossible to decide whether the stenosis exists at the pylorus or just below it, and whether the case was primarily one of duodenal or of gastric ulcer. The only clue to aid in a decision will be the early history of the case, before stenosis developed. The following case shows the difficulties in diagnosis when this complication exists:

CASE III.—Mrs. A., aged thirty-five years, was referred to me in August, 1908, by Dr. Huffaker, of Carson, Nevada. For years past she had a history of sour stomach, belching of gas, heartburn, and distress after food, relieved by taking soda. In January, 1907, she began to have more serious trouble, characterized by attacks of pain in the upper abdomen, running through to the back, and by frequent vomiting of very sour material. In October, 1907, when she consulted Dr. Huffaker about these symptoms, he found an enormously dilated stomach, with much food retention. With daily lavage and suitable diet, however, she improved greatly, and remained fairly well until three months before I saw her. Then there was recurrence of the pain and vomiting, with gradual loss of weight and strength. The examination showed definitely a protrusion of the abdomen due to a dilated stomach, with loud succussion splash, and the greater curvature 6 cm. below the navel. On introducing the stomach tube, about twelve ounces of very foul-smelling semisolid debris escaped, and many washings failed completely to cleanse the organ of food refuse. In the right hypochondrium a hard and very tender mass was palpable, the size of a hen's egg; and peristaltic waves ran across the stomach from left to right, visible and palpable. Ultimately, after several days of lavage, a test meal was given, showing on analysis a total acidity of 60, with the free HCl 36. The feces showed occult blood persistently, and at times were ink black for a day or two. The patient never vomited blood, nor did the stomach contents ever give the reaction for occult blood. After several weeks study of the case, operation was advised and was performed by Dr. Stanley Stillman. It revealed an old ulcer in the duodenum, about one inch beyond the pylorus, with much thickening, cicatrization, and stenosis. Following gastro-enterostomy, the patient made a perfect recovery and has since remained well.

3. *Hemorrhage* from duodenal ulcer is an accident and a late complication, and the diagnosis should be made long before it occurs. When it does take place, it adds to the typical clinical picture, as described, the story of sudden attacks of faintness, pallor, and sweating, perhaps even of actual loss of consciousness, followed sooner or later by the discharge of black, tarry stools. Slight oozing of blood from the ulcer base is not unusual at the time of and following one of the characteristic attacks of pain; but this gives rise to no gross discharge of blood in the feces, recognizable

by the naked eye, and chemical tests for occult blood are required to demonstrate its presence. Actual hemorrhage, on the other hand, not only produces symptoms of anemia and collapse, but the stools for days afterward may be black and sticky and manifestly, even to the patient, of a very unusual character. The blood from a duodenal ulcer is rarely vomited, but escapes through the bowel, and no vomiting at all may occur at the time of the hemorrhage, although nausea is frequent from faintness and cerebral anemia. Such an addition to the patient's story rather makes the diagnosis plainer, but it is not a part of the usual course and is not to be awaited before a diagnosis is reached. The following cases show what is to be expected when hemorrhage complicates duodenal ulcer.

CASE IV.—Mr. P., aged forty-seven years, consulted me in June, 1910, because a week before, in the afternoon, after feeling well all day, he was taken suddenly ill with nausea, dizziness, faintness, and profuse sweating, the whole attack lasting about two hours. There was no pain with the attack and no vomiting. For three days following that he felt well. Then the same attack recurred—nausea, faintness, and profuse sweat, finally leading this time to loss of consciousness. The next day he noticed that the discharge from the bowel was black, and it had been so each day since. Ever since the last attack he had felt very weak and faint. On questioning him it was found that for fifteen years, off and on, he had had spells of what he called “simply indigestion,” characterized by ferocious pain in the stomach, running through to the back, coming on every day for a month or so at a time, then gone for several months, during which he felt well; this pain always occurred several hours after food, and eating would relieve it temporarily; he always had a good appetite and never vomited or felt like it. Examination showed a marked anemia, with the hemoglobin 60 and the red corpuscles 2,950,000; occult blood repeatedly present in the stools; a decided hyperchlorhydria, with a total acidity of 84 and free HCl 72; but no abnormality on physical examination of the abdomen, in the stomach, liver, or spleen. Gastroenterostomy was advised but refused.

CASE V.—Mr. L., aged thirty-four years, entered my service in Lane Hospital in February, 1910, because his stools were black and tarry, and he had much pain in his stomach. The black passages recently had frightened him and led him to seek advice, but for several years previous he had had recurring attacks of pain and distress in the upper abdomen, usually commencing about three hours after eating and relieved by taking more food. Between such attacks he was fairly well. The present illness had lasted a month, with pain most severe at night, in the epigastrium, radiating through to the back. He never vomited. Examination showed fulness, rigidity, and tenderness in the left costal groove; a suc-

cussion splash over the stomach; no palpable mass; no dilatation of the stomach; the liver and spleen normal in size. The feces were black and tarry and showed an abundance of blood. The test meal showed a total acidity of 160, free HCl 60, and combined HCl 70. Operation by Dr. Stanley Stillman showed an ulcer in the duodenum, approximately one inch below the pylorus. Gastro-enterostomy was performed and the patient made a good recovery—though after leaving the hospital he went on a debauch and many of his symptoms then recurred.

4. *Perforation* of duodenal ulcer is, of course, an unexpected event, and rarely occurs as the first manifestation. A more or less lengthy history of the characteristic attacks of pain usually precedes this disaster. Yet it may come as the first incident that causes the patient to demand professional care, and in any event there is usually no time to elicit a careful clinical history in the face of such a grave complication. The immediate symptoms of perforation, whether of the stomach or duodenum, are very much the same—violent pain coming suddenly in the upper abdomen, pallor and faintness, cold sweat and rapid respiration, with rigid and tense abdominal wall, extremely tender, particularly in the upper half. However, if time can be taken to elicit a careful clinical history, it is possible to decide whether the ulcer has been duodenal or gastric. But this, as a rule, is not practicable, and fortunately, the same operative procedure is indicated in either case.

But the difficulties of diagnosis do not cease when complications are excluded. The characteristic feature of chronic duodenal ulcer is recurring attacks of pain in the upper abdomen, and there are two other common conditions that give rise to similar attacks—gastric ulcer and cholelithiasis. We have now to inquire how to distinguish duodenal ulcer from each of these.

1. *Gastric Ulcer*. Is it possible to tell when an ulcer lies above and when below the pyloric ring? For years it has been considered sufficient to make the diagnosis of ulcer, without attempting to decide its exact location, leaving the surgeon to settle this at the operating table. And yet differentiation is possible, and close attention to the clinical history and physical signs makes accurate localization before operation almost a certainty in uncomplicated cases. Both gastric and duodenal ulcer give a long-continued history of painful attacks in the upper abdomen, recurring at varying intervals; but in gastric ulcer there is much more likely to be a persistent acid dyspepsia in the period between attacks—characterized by sour stomach, burning distress, water brash, flatulence, and nausea; and nutrition is in consequence more frequently disturbed. As regards the attacks themselves, the site of pain may be the same in either, the radiation is usually through to the back no matter whether the ulcer is gastric or duodenal, and the character of the suffering is the same in each. The most

important difference between the two is the time at which the pain begins—in gastric ulcer very shortly after food is taken or almost invariably within the first two hours after; not coming habitually in the night, arousing the patient from sleep. In gastric ulcer also the pain is accompanied almost, as a rule, by nausea, persisting and increasing until vomiting removes the offending stomach contents and so gives relief. In general, the symptoms of stomach disturbance are more marked and frequent in gastric than in duodenal ulcer; both during and between the attacks of pain.

On physical examination, again the signs of gastric disturbance are the striking ones when the ulcer is in the stomach. A succussion splash several hours after food, evidence with or without inflation that the stomach is dilated, a peristaltic wave across the stomach wall, a tender area limited to the site of pain, rigidity of the rectus and increased reflex over it in one or the other hypochondrium—all of these signs are frequently found in gastric ulcer, in marked contrast to the lack of physical signs in duodenal ulcer. The test meal shows hyperchlorhydria almost invariably, and frequently very high HCl values, and occult blood in the stomach contents after a test meal is not uncommonly found, as it practically never is when the ulcer is below the pylorus. Einhorn⁸ has proposed as a differential test a small gold bucket, which the patient swallows in the evening and retains over night. To this is attached a long silk thread, by which the bucket is withdrawn in the morning. The bucket finds its way during the night into the duodenum, and when again withdrawn the silk thread is examined for blood stain. If such a stain is found, its distance from the lips affords a guide as to the site of the bleeding area. Einhorn is enthusiastic about this test, and thinks it an important aid in differentiating gastric from duodenal ulcer. I have used it in a few cases, but not in enough to have reached a conclusion about its value.

Gastric ulcer likewise has hemorrhage as a complication, but the blood then is usually vomited, while in duodenal ulcer it escapes by the bowel. Some of the blood poured out into the stomach, however, escapes into the bowel and so produces melena as well as hematemesis, but hematemesis is the striking feature of the hemorrhage. In the hemorrhage from a duodenal ulcer, on the contrary, some of the blood may regurgitate into the stomach and be vomited, though rarely, but the most of it escapes by the bowel and melena here becomes the characteristic event. In case hematemesis and melena are both profuse, the suspicion should be of an ulcer lying across the pylorus, partly gastric and partly duodenal.

2. *Cholelithiasis*. Attacks of hepatic colic cause even more difficulty in differential diagnosis than does gastric ulcer. Nevertheless, there are certain characteristics about the history that make

⁸ AMER. JOUR. MED. SCI., 1909, cxxxviii, 162.

differentiation at least a possibility. As with duodenal ulcer, the attacks recur throughout many years, coming six months or a year apart, or once a month, or even more frequently still. In the interval the patient may feel perfectly well or may suffer from chronic dyspepsia. But the nutrition is usually well preserved, and the patient with chronic cholecystitis is often fat or even obese. So far, then, there is no differentiating symptom. But when we come to analyze the painful attacks themselves, we find essential differences from what is observed in duodenal ulcer. The site of pain when the attack begins may be in the epigastrium, but the radiation is quickly to the right costal margin, around into the back and underneath the right shoulder blade. The pain, furthermore, is distinctly colicky in character, with remissions and exacerbations, coming on more suddenly and ceasing more abruptly than the pain of either duodenal or gastric ulcer. In its severity it is always more intolerable and the suffering it causes is more intense. As regards its time of onset, it may begin in the night, arousing from sleep, like the attack of duodenal ulcer, but it may also come on at any time during the day, regardless of whether food has been taken recently or not. It lasts a variable time, one hour or several, but it is not relieved by taking food or alkalies, nor by vomiting, and usually requires morphine because of its severity. While the attack lasts, the patient often feels chilly, sweats profusely, is nauseated, and vomits; frequently there is slight elevation of the temperature, and in about half the cases more or less jaundice after the attack is over. In many details, therefore, the attacks of cholelithiasis, when closely analyzed, differ essentially from those of duodenal ulcer, and the clinical history becomes of the first importance in differential diagnosis.

As regards physical examination, shortly after an attack this will show tenderness and rigidity, not in the epigastrium, but at the right costal margin, especially after a deep breath, and at times a palpable mass there corresponding to the site of the gall-bladder though usually tenderness is too great and the rectus muscle too rigid to permit deep palpation to be made. At another time, when there has been no recent attack of pain, the physical examination may be quite as negative as in duodenal ulcer. In uncomplicated cases, without adhesions between gall-bladder and pylorus, there are no evidences of food stasis in the stomach or of gastric dilatation. The test meal may show a marked hyperchlorhydria in gall-bladder disease, and this must not mislead. In other cases the stomach analysis may give a normal or subnormal amount of HCl, so that while an excess may occur with chronic cholecystitis as well as with chronic gastric and duodenal ulcer, normal acidity does not negative the diagnosis in any one of the three. Occult blood in the feces does not occur with gall-bladder disease, unless complicated by some other condition; and its presence repeatedly

on examination, in a doubtful case, would speak against cholelithiasis or cholecystitis as a cause of the painful attacks.

It is by careful attention to such details as have been described, in clinical history, physical examination, and laboratory tests, that we seek to distinguish duodenal ulcer from other conditions that resemble it. Usually it is possible, if only sufficient time is taken to collect, to sift, and to weigh the facts. No claim is made that the diagnosis is easy or that errors never occur. The only diagnostician with perfect confidence in himself is the one who never sees his conclusions checked up by the surgeon or the pathologist. After all, we can only do our best to reach the truth in diagnosis as in every other work in life, and our only concern must be to do our best.

OBSERVATIONS ON TRAUMATIC DIABETES IN CHILDREN.

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Two cases of diabetes have recently come under our observation in the children's wards of the Michael Reese Hospital. In both cases the glycosuria first came to light after the patients had suffered injury. As will be observed from the histories, the first child sustained injuries to the leg and abdomen in an automobile accident; the second child fell from a second story window, striking on his head. In addition to the possible traumatic origin of these cases, there is an added interest in that both patients continue robust and in good health in spite of the daily elimination of a considerable quantity of sugar. This is in contrast to the text-book descriptions of cases of diabetes in children, which usually relate that young individuals, more particularly children, who are suffering from diabetes run a rapidly unfavorable course.

It will also be of interest in studying the case histories to note the effect of the von Noorden oatmeal diet on sugar elimination and acid retention. In the second case especially we were able to make fairly complete studies on the carbohydrate and nitrogen metabolism, the results of which, while presenting nothing startlingly new, are nevertheless of considerable interest. This will be discussed later,

CASE I.—The patient, D. R., aged eleven years, of Russian Jewish parentage, was admitted to the surgical department of the Michael Reese Hospital, July 2, 1907, with the following history: While walking in the street the patient was struck from behind by an automobile. He fell unconscious and remained so for about thirty minutes. On reaching the hospital he had regained consciousness, his mind was clear, and no evidences of head injury were found, but there was a compound fracture of the right tibia. Under ether anesthesia the wound was cleansed and the fracture set by Dr. L. A. Greensfelder. The recovery was uneventful, and after five weeks the boy was discharged in good condition. The urine was normal on the day following the injury.

About eighteen months later, January 19, 1909, he was again admitted to the Michael Reese Hospital, this time to the medical service of Dr. Abt, with the following history: Last February (eleven months ago, and seven months after the injury) the boy began to be troubled with marked diuresis. Nine months ago he was urinating about twelve times a day, three-quarters of a quart at a time. His appetite became enormous and his thirst increased until he has required about fourteen cups of water daily for the last four months. He has grown progressively weaker and his eyesight is becoming poorer. Aside from a dryness in the throat and an occasional headache of late, he has been feeling well. He had measles seven years ago, but has otherwise enjoyed good health. The family history is negative, showing no constitutional diseases or neuroses.

Examination. On physical examination nothing abnormal was found except diminished patellar reflexes. The blood picture and blood pressure were normal, and nothing abnormal was found by Dr. Snyder in the eye-grounds. One hundred and six ounces (3180 c.c.) of urine were voided in twenty-four hours, showing 5.4 per cent. of sugar and the presence of acetone, but no diacetic acid.

Treatment and Reaction. He was given a restricted diet until April 21, a period of about three months, the following being an average daily diet:

8 A.M. Orange, egg, bacon, and coffee with cream.

10 A.M. Broth, 6 ounces.

Noon.¹ Gluten bread, salad, steak, tea, and dessert.

3 P.M. Orange.

5 P.M. Steak, chicken, or chop, gluten bread, tea with cream, and custard.

In addition, thymus gland, both dry and glycerin extract, was administered for about five weeks and Fowler's solution for about three weeks, without any noticeable effect. During this period the urine averaged 1000 to 1200 c.c. in twenty-four hours and constantly contained from 1.4 to 6.5 per cent. of sugar, and usually acetone,

¹ The gluten bread which was used contained 32.5 per cent. carbohydrate.

but no diacetic acid. His weight in the last month averaged about seventy-two pounds. His appetite improved and his weakness became less pronounced.

He was then given green vegetables alone for two days, but the sugar remained high and the weight dropped to seventy-one pounds. The general diabetic diet was resumed for six days, but the boy lost two more pounds and the sugar averaged 4 per cent.

On May 5, in spite of the loss in weight, the diet was limited to the von Noorden gruel, prepared according to the following formula: Oatmeal, 250 grams; butter, 250 grams; the whites of six eggs; salt to flavor. To be consumed in twenty-four hours.

The sugar promptly disappeared and remained absent, but acetone was constantly present. After four days green vegetables were added to the diet and sugar remained absent, but the weight fell to sixty-six and one-half pounds. After a week of the gruel the general diet was again resumed, and the sugar promptly rose to 6.1 per cent., and with it the body weight increased to seventy-two pounds.

After ten days of the liberal diet, von Noorden's gruel was again given for about a month, a period from May 16 to June 13, from 200 to 400 grams of green vegetables being added after the first week. Sugar was absent during this period, but acetone in various amounts was usually found. The weight fell at first and then remained fairly constant, averaging 66 to 68 pounds. The boy felt well, although acetone was constantly present; his hunger was satisfied, and he found the gruel not distasteful. Casts were found in the urine at times during this period, and the total amount of urine varied from 500 to 1200 c.c.

Beginning June 13, meats and oranges were gradually added, and the weight rose from 66 to 70½ pounds. Sugar remained absent from May 16 until June 25, and from that time until July 9 varied from 0 to 5 per cent. An average diet (June 20) was as follows:

8 A.M. Gruel, 155 grams; coffee, 125 grams; half of an orange.

Noon. Vegetables, 275 grams; gruel, 190 grams; beans, 90 grams; chicken, 140 grams.

3 P.M. Gruel, 160 grams.

5 P.M. Beans, 100 grams; gruel, 175 grams; vegetables, 190 grams.

Ten days later, July 1, the diet was as follows:

8 A.M. Bacon, 70 grams; gruel, 210 grams; coffee, 210 grams; half of an orange.

Noon. Green vegetables, 245 grams; scraped beef, 60 grams; chicken, 100 grams; gruel, 140 grams.

3 P.M. Gruel, 240 grams.

5 P.M. Vegetables, 280 grams; beef, 90 grams; gruel, 234 grams.

On July 8 a piece of toast was added, and the sugar rose to almost 3 per cent. On July 12 the toast was stopped, and the sugar fell

to 0.6 per cent. On July 15, he left the hospital, feeling well, voiding about a quart of urine daily, containing less than 2 per cent. of sugar, some acetone, but no albumin or casts.

Since leaving the hospital he has been on a general diabetic diet, with gluten bread (no wheat bread, potatoes, or sugar). His weight increased gradually from 70 pounds to 79 pounds August 15, 1910. A urinalysis once or twice weekly showed the presence of less than 2 per cent. of sugar, averaging less than 0.5 per cent. for the past month. His general health has remained good, and he feels no pain or discomfort, in spite of an almost constant acetonuria.

Chart I, prepared by Dr. Jampolis, shows graphically the course of the disease in this patient.

CASE II.—Isadore F., aged thirteen years, a schoolboy, of Jewish American parentage, was admitted to the Michael Reese Hospital January 10, 1910.

Personal History. Was born at full term. Labor normal. No complications at birth. Breast-fed for two and one-half years, gaining steadily all the time. Dentition began about the fourth month, normal order of eruption. No nervous or digestive disturbances during this period. Could sit up at three months, walk at ten months, talk at eleven months. Muscular and mental development normal up to present illness. At four years of age he had measles, following which he had discharge from both ears, which lasted for about three years. Had scarlet fever soon after he recovered from the measles. Has occasional tonsillitis.

Present Illness. Dates back to three months ago, when he fell from a second story window, landing on his head. Since that time his appetite has been steadily increasing, eating about twice as much as formerly. Has a mania for sweets. He also has polydipsia, sometimes drinking twenty to twenty-five glasses of water daily. Associated with this, he commenced to pass large quantities of urine and at short intervals, occasionally passing seven quarts in twenty-four hours. He is compelled to get up several times at night to urinate. Has lost about 10 pounds in weight in the last four weeks. Complains of feeling weak and tired all the time. The last few days has been complaining of pains in the legs. Has occasional headaches. No visual disturbances. Bowels are constipated.

Family History. Mother living; had two other children, who died of unknown cause. Had one miscarriage after the patient was born—at fourth month. No history of diabetes or hereditary disease in family.

On Admission. Fairly well-nourished boy; is somewhat pale-looking; dry lips. Lies quietly in bed, apparently not in pain. Scalp negative. Over right frontal eminence is a bony elevation, 2 cm. in diameter and 2 mm. in height, pressure over which causes considerable pain. Ears negative; no signs of mastoid disease.

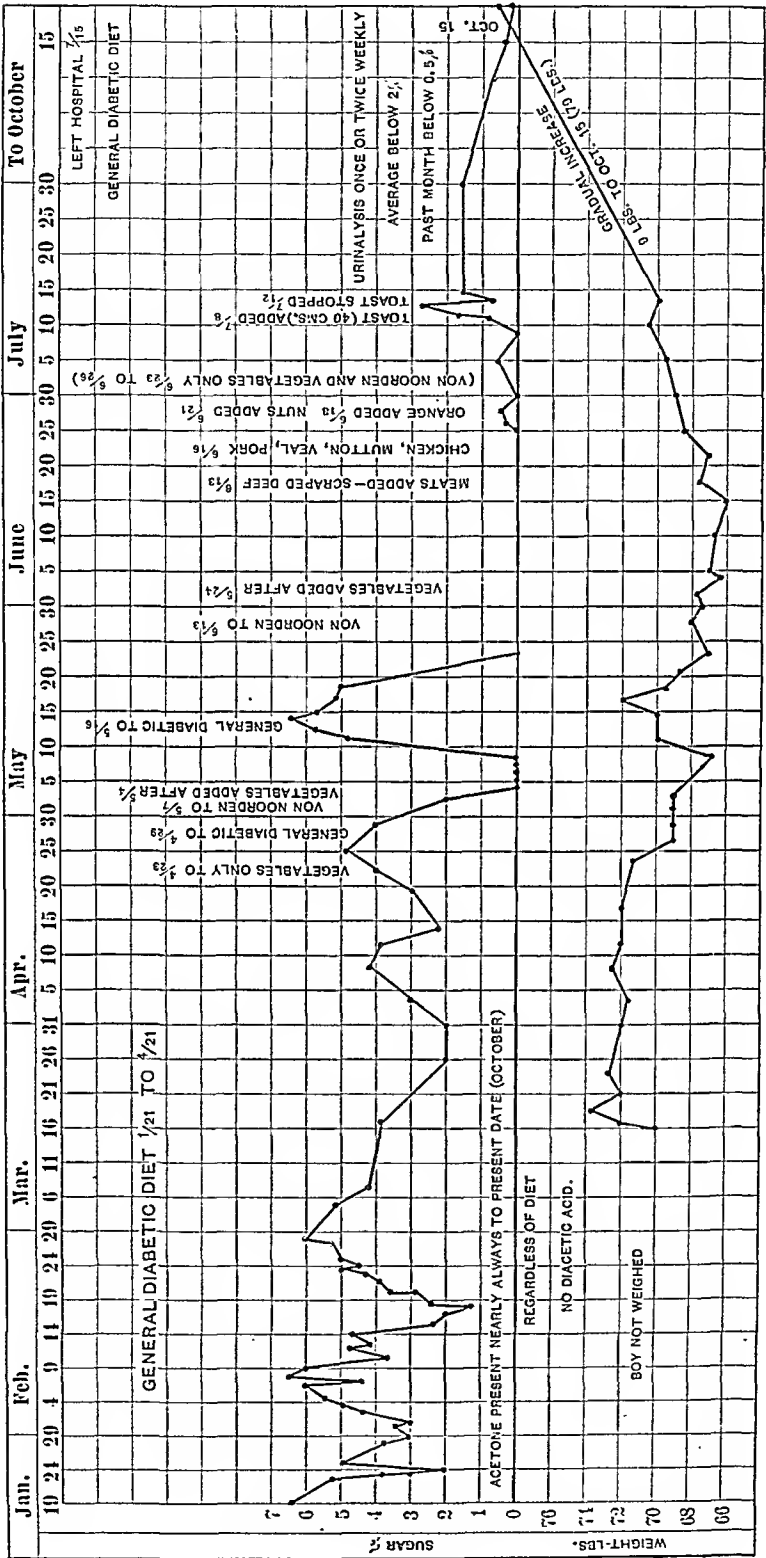


CHART I.—Illustrating the course of Case I.

Eyes: Vision good; pupils regular; react to light; accommodation. Fundus normal. Nose negative; no obstruction to breathing. Mouth: Lips dry and slightly anemic; tongue has thick, grayish coating; tonsils enlarged but not inflamed. Neck: Few palpable lymph glands in posterior triangle. Face: Linear vertical scar over right malar region, extending down over right cheek. Thorax: No deformities. Lungs negative. Heart: Palpation and percussion negative. On auscultation, a very faint blowing systolic murmur is heard at apex; not transmitted to axilla. Second pulmonic not accentuated. Abdomen: Moderate tenderness on deep pressure over right hypochondrium; abdomen flat; not tympanitic. Extremities negative; reflexes normal.

January 22, 1910. Patient has an erythematous rash covering abdomen, limbs, and face. Itches considerably.

January 31, 1910. Has had severe toothache for two days; relieved by application of oil of cloves. Complains also of burning sensation in eyes. Vision not impaired.

March 3, 1910. Has fits of despondency. Folliculitis on back of scalp.

March 13, 1910. Has catarrhal tonsillitis.

March 29, 1910. Mental state cheerful.

April 6, 1910. Marked tenderness in right hypochondrium. Slight resistance felt just beneath costal arch, seventh rib. No jaundice.

April 7, 1910. Vomited several times.

April 16, 1910. Feels drowsy. Patellar and abdominal reflexes markedly exaggerated.

April 17, 1910. Feels bright; no nausea. Still tender over gall-bladder region.

April 23, 1910. Furuncle in right external auditory canal opened.

Laboratory Findings. On admission, January 10, 1910: White blood corpuscles, 8500; red blood corpuscles, 5,856,000; hemoglobin, 90 per cent. (Dare). von Pirquet tuberculin reaction positive. Differential count of the leukocytes: Polymorphonuclear neutrophiles, 41 per cent.; small mononuclears, 48 per cent.; large mononuclears, 1 per cent.; transitionals, 2 per cent.; eosinophiles, 8 per cent.; basophiles, 0 per cent. A throat culture shows no Klebs-Loeffler bacilli. An analysis of the twenty-four-hour specimen of urine shows 3 per cent. of sugar, no acetone, and no diacetic acid.

January 14, 1910. Patient on practically the same diet as Case I, and receiving Fowler's solution, 2 drops after meals.

Urine analysis: Sugar, 2.99 per cent.; diacetic acid and acetone absent.

January 20, 1910. Same dietetic and medicinal treatment. Urine analysis: Twenty-four-hour specimen, 850 c.c. Sugar, 2.41 per cent.; a trace of acetone; no diacetic acid.

February 1, 1910. Twenty-four-hour specimen of urine, 1920 c.c. Sugar, 4.08 per cent.; a trace of acetone and diacetic acid.

February 3, 1910. Given von Noorden diet. Twenty-four-hour specimen of urine, 2040 c.c. Sugar, 1.8 per cent.; marked acetone and diacetic acid.

February 6, 1910. Put on full diet. Twenty-four-hour specimen of urine, 4530 c.c. Sugar, 4.1 per cent.; acetone, faint trace; diacetic acid, marked.

February 9, 1910, to March 4, 1910. On restricted diet. Sugar in urine ranges from 2.8 per cent. to 3.75 per cent. No acetone or diacetic acid. Weight, $76\frac{1}{4}$ pounds. Lost 1 pound.

March 4, 1910. Von Noorden's diet. Weighs $78\frac{1}{2}$ pounds. Twenty-four-hour specimen of urine, 1230 c.c. Sugar, 1.3 per cent.; acetone present; diacetic acid absent.

March 5, 1910. Von Noorden's diet. Twenty-four-hour specimen of urine, 450 c.c. No sugar; acetone present; diacetic acid absent.

March 6, 1910. Diabetic diet. Twenty-four-hour specimen of urine, 900 c.c. Sugar, 1.7 per cent.; acetone and diacetic acid absent.

March 7, 1910. Diabetic diet. Sugar, 1 per cent.; no acetone or diacetic acid.

March 10, 1910. Von Noorden's diet. 900 c.c. of urine in twenty-four-hour specimen. Sugar, 1.8 per cent.; acetone present; no diacetic acid.

The diet and the urinalyses from March 21, to April 10 will be presented and discussed in the tables.

From April 10, 1910, to June 22, 1910. On restricted diet. Sugar ranges from 1 to 3 per cent.; acetone present in faint traces; no diacetic acid. Weight, 81 pounds. Urinates on the average about 2500 c.c. in twenty-four hours.

From June 23 to July 10 further metabolism studies were undertaken; these will be discussed later.

That trauma to the head and spinal column may produce transitory and permanent glycosuria has been recorded for a long time. Griesinger² was the first to note that severe trauma to other parts of the body, as the muscles and abdomen, may be followed by diabetes.

In the review of 212 cases of head injuries admitted to the Boston City Hospital, Higgins and Ogden³ found glycosuria in 20 cases—5 being simple scalp wounds, 4 deeper wounds denuding the bone, 5 fractures of the vault, and 5 fractures of the base.

Professor von Noorden has furnished to the Imperial Insurance Office an interesting report of the etiological connection between an

² Cited from Kleen, *Diabetes and Glycosuria*.

³ *Boston Med. and Surg. Jour.*, February 28, 1895

injury and a severe diabetes mellitus, which ran its course to a fatal termination in about ten months. A laborer received a severe blow on the head from a heavy piece of iron, which was followed by nose-bleed, giddiness, and temporary confusion. About three months after the accident a severe diabetes began, which ran a very rapid and fatal course. The occurrence of nosebleed indicates, according to von Noorden, an injury to the bones of the base of the skull. While the trauma was not great, concussions of the brain without anatomic lesion are, however, the most frequent causes of traumatic diabetes. In consideration of the fact that he has never seen a slowly developing and latent diabetes suddenly develop in an otherwise vigorous man to an especially severe diabetes, von Noorden comes to the conclusion that the diabetes was produced by the accident. The Imperial Insurance Office has therefore awarded to the survivors of the unfortunate man the required income.

According to Naunyn, although the traumatic glycosurias are, as a rule, the most favorable, nevertheless some of the most severe cases are of traumatic origin. He questions the right of anyone to deny that the frequent transitory glycosurias are manifestations of a true diabetes. Finding an hereditary influence in a large number of cases in all types of the disease, he recognizes only two forms—the “mild” and the “severe,” the pathogenesis in all cases being a hyperglycemia. Ebstein also believes that in all cases of traumatic diabetes individual predisposition is an important factor. He collected from his own clinic and the literature 50 cases of traumatic diabetes, half of which were due to head injuries and half to injuries elsewhere. The predisposition of the Jewish race to diabetes is well known, and it is of interest to note that both of our cases of traumatic diabetes were in Jewish children.

In our cases the traumatic origin of the disease and the fact that both cases ran a much milder course than is usually pursued by diabetes in children, prompted some simple metabolism studies to determine whether there existed any differences from the usual disturbances in this disease. Inasmuch as the ordinary clinical study of the first case showed an apparent anomaly in the production of an acidosis by the von Noorden gruel, this point was especially investigated in Case II. For certain periods the patient was allowed a somewhat restricted diet, containing gluten bread, supposedly starch-free, but actually, on analysis in this laboratory, yielding 32.5 per cent. starch. For the first ten days the food was not measured accurately enough to allow complete figures of food values to be stated; but from March 21 to April 9 each article was carefully weighed and its value computed, mainly from Atwater's tables, partly from analyses made in this laboratory. Very little restriction, except of carbohydrate, was enjoined during the period of liberal diet, and at all times the patient was allowed to roam about the wards, under surveillance, to prevent secret taking of food or loss

of urine. Tables showing in detail the quality and quantity of food taken, total calories, protein, fat, carbohydrate, and water ingested, are presented. The urinary analyses were those which can be performed in any clinical laboratory. The sugar was determined by the Benedict copper reduction, the total nitrogen by the Kjeldahl, ammonia by the Malfatti, acetone qualitatively by both the sodium nitroprusside and iodoform tests, and diacetic acid by ferric chloride. The figures in Table I, showing the results of these analyses, are self-explanatory, but their interpretation permits of some discussion.

The absolute reduction in sugar output as soon as the patient is put on von Noorden's gruel is striking, and is in perfect accordance with the claims of von Noorden and the experiences of other workers. With the von Noorden gruel the patient received more carbohydrate than he did during the liberal period, but only in one form. Croftan⁴ and Herrick⁵ have both seen examples where this diet in children was of exceptional benefit, not only in reducing sugar output, but also in diminishing acidosis. In both of our cases, however, acetone, which was practically never present during the periods of glycosuria, invariably appeared after the exhibition of the oatmeal gruel. Clinically associated with this were symptoms suggesting acidosis, such as nausea, rapid pulse, and headache; the ferric chloride reaction, however, generally was absent. Since it is very unusual for an acidosis to follow the use of von Noorden's gruel, it was thought that the quantitative determination of the nitrogen and ammonia output might explain the apparent deviation from the usual reported reaction. The chart shows a relative increase of ammonia each time the von Noorden diet is given, but as the nitrogen excretion always fell markedly because of a low protein intake, it is probably more important to consider the absolute ammonia figures before concluding that the high NH_3 percentage signifies acidosis. The figures representing total ammonia vary considerably and are not in agreement with the percentage curve. In fact, during the periods from March 16 to 20, and from March 25 to 26, when the NH_3 was 10 per cent. of the total nitrogen, the actual ammonia output was lower than it was at any other time during the period of observation. It is probable that the increased ratio is due to the low total nitrogen excretion, corresponding to the sudden diminution in the nitrogen intake. But the figures at the first and last von Noorden period show an absolute increase of ammonia. On March 13, after three days of the gruel, 4 grams of NH_3 , or 22 per cent. of the total nitrogen, was excreted in the urine, and with the reduction in the glycosuria after the gruel on April 6, the actual as well as the relative ammonia elimination was increased.

In attempting to explain this, one can immediately exclude the carbohydrate as having any causal connection, as a larger amount

⁴ Jour. Amer. Med. Assoc., 1909, lii, 1313.

⁵ Ibid., 1908, i, 862.

TABLE I.

March, 1910.	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Apr. 1	2	3	4	5	6	7	8	9	
Meat.	+	+	+	+	+	+	352	164	150	325	132	310	104	165	293	370	340	77	67	157	25	
Eggs	+	+	+	+	+	+	177	60	110	90	310	282	289	325	125	456	143	125	319	275	142	
Vegetables	+	+	165	27	285	100	450	100	167	190	125	0	0	42	100	65	
Butter	+	+	+	+	+	+	20	20	10	5	15	88	34	65	26	77	40	23	24	24	10	
Gluten bread	+	+	+	+	+	+	162	134	123	33	100	427	86	220	95	200	90	95	75	135	40	
Potatoes	+	+	+	+	+	+	50	..	10	18	30	74	17	23	
Cheese	80	50	10	840	225	154	57	110	300	166	195	155	170	100	
Cream	+	+	+	+	+	+	570	1080	1450	240	2020	805	1035	1620	980	1285	1320	837	868	1305	1100	
Milk	+	+	+	+	10	7	90	75	85	10	
Nuts	15	16	30	43	33	
Olives	
Soups	+	+	+	+	200	87	265	360	522	505	300	360	330	300	408	400	256	780	635	432	2125	
Water	+	+	+	+	+	+	+	+	+	+	1332	1617	2580	1214	1620	942	3646	2675	2010	3200	2300	2390	2340	2660	2200	2110	
von Noorden	500	500	..	166	..	83	333	500	166	332	500	332	
Protein	146	95	116	77	32	21	209	207	147	181	122	203	149	132	142	171	31	30	31	76	
Fat	168	132	122	383	230	153	189	257	165	227	226	862	222	182	185	207	230	230	230	87	
Carbohydrate	91	96	121	113	150	100	163	210	91	157	93	140	100	94	86	127	144	141	143	69	
Nitrogen	23	13	18.5	12.2	5.0	3.3	33.5	33.1	23.4	28.9	19.3	32.5	23.8	21.1	22.7	27.3	4.9	4.8	4.9	12.1	
Calories	2132	2017	2093	4339	2886	1917	3288	4097	2505	3497	2969	4765	3087	2614	2651	3151	2857	2846	2851	1403	
Weight: Showed variations of one or two pounds throughout the period of observations.																															
Total urine	2760	1560	1950	2370	1440	510	625	600	1380	930	1710	2010	810	540	840	1560	2220	2225	2340	1840	1950	1590	1950	2370	2400	870	720	660	1080	
Spec. gravity	1023	?	1027	1031	1027	1021	1016	1019	1016	1017	1020	1021	1030	1020	1024	1023	1022	1027	1032	1024	1032	1032	1032	1026	1031	1031	1023	1026	1020	1020
Sugar, p. c.	0	0	2.68	3.0	1.78	0	0	0	0.63	0.63	1.17	1.36	1.25	0	0	0	1.2	1.88	2.68	2.42	2.58	3.75	3.75	2.0	2.6	1.5	0	0	0	0
Sugar, grams	0	0	50	70	25	0	0	0	9	5	20	28	10	20	0	0	0	26	40	62	45	50	60	74	44	62	14	0	0	0	0
Acetone.	+	+	+	0	0	+	+	+	+	±	0	0	0	+	..	+	0	0	0	0	..	+	+	±	0	+	+	+	+	+
Diacetic acid	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0
Ammonia	4.04	2.7	1.96	1.45	1.58	0.52	0.55	0.83	1.57	0.72	1.08	0.96	0.63	0.44	0.89	2.13	1.27	1.06	1.59	1.44	1.46	0.86	1.19	1.41	1.18	0.86	1.27	1.58	2.16	2.16
Nitrogen	17.7	15.7	16.16	20.1	18.5	6.57	5.90	6.32	13.21	6.85	17.28	15.76	10.95	4.84	7.5	22.7	1.79	18.0	24.7	19.9	22.2	15.48	21.7	22.8	22.3	11.1	8.4	7.8	12.0	12.0
NH ₄ N, p. c.	22	18	12	7	8	8	9.5	12.5	12	10	6	6	5.6	9	12	9	7	6	6	7	6	5	5	6	5	8	15	20	18	18

TABLE II.

June, 1910.	23	24	25	26	27	28	29	30	July 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Ment . . .	250	200	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250
Eggs . . .	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200
Vegetables . .	300	265	360	230	350	2888	1635	150	150	150	2057	2150	400	400	400	400	400	400	400	400	400	400	400	400	400	400	
Butter . . .	75	90	125	150	150	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	
Tonst . . .	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	75	
Potatoes . . .	1320	1610	1900	1440	2000	2160	2160	2800	2200	2340	1200	1840	2680	1950	3620	4020	4620	4320	5000	4220	4400	4620	4620	4420	3920	5320	
von Noorden	357	500	500	
Sod. bicarb.	8	12	16	30	30	30	30	30	28	24	20	24	28	30	30	30	30	30	30	30	30	30	30	30	30	30
Protein . . .	75	67	76	73	76	48	29	35	50	50	39	37	71	71	82	74	75	78	77	78	78	88	88	77	75	78	
Fat . . .	125	130	167	187	187	7.8	4	175	248	248	2.5	5	187	187	145	150	148	145	146	146	146	147	147	146	146	146	
Carbohydrate . .	40	40	58	47	57	144	38	99	138	138	106	105	17.5	17.5	39	49	45	63	60	77	77	130	130	60	61	51	
Nitrogen . . .	12	11	12	12	12	7.08	4.6	5.5	4.1	4.1	6.1	6	11	11	13.2	11.8	12	12.3	12.3	12.3	12.3	14.1	14.1	12.3	11.9	12.3	
Calories . . .	1674	1692	2101	2235	2286	858	517	2171	3074	3074	615	629	2094	2094	1848	1900	1870	1926	1920	1985	1985	2265	2265	1920	1905	1917	
Weight of patient . .	{ 83.5	79.5	82.5	80.5	80.5	81.5	79
Weight in kilos . .	{ 83.5	36	27.5	..	37	36.6	36.6	37	35.9
Total urine . .	1680	1740	1860	1875	1755	2430	2350	1775	2125	2125	1900	2275	4050	3400	3210	2550	3060	2760	3840	4350	4140	4080	4260	..	3180	4920	4800
Spec. gravity . .	1035	1032	1026	1032	1024	1023	1018	1017	1015	1009	1012	1014	1012	1010	1006	1016	1015	1015	1012	1012	1008	1018	1013	..	1013	1010	1010
Sugar, per cent. .	1.3	2.3	3.26	2.58	2.1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0.5	0.5	1.6	1.5	..	0.5	0	0
Sugar, grams . .	22	41	60.6	48	39	24	0	0	0	0	0	0	0	0	0	0	0	0	0	21.7	20.7	65.28	63.9	..	15.9	0	0
Acetone . . .	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	0	0	+	..	0	+	+
Diacetic acid . .	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	0	0	+	..	0	0	0
Ammonia . . .	8.68	5.1	5.06	2.68	14.65	2.1	2.1	0.84	1.5	1.65	1.23	0.65	1.36	1.8	2.03	0.45	5.5	4.8	4.9	3	3.9	6.73	8.2	..	5	6.5	4
Nitrogen . . .	15.5	18.51	16.16	18.11	15.72	10.2	6.7	4.97	6.25	7.32	5.32	4.91	7.71	11.06	?	10.3	13.7	10.3	14.2	15.3	15	14.2	16	..	12.5	14	12
NH ₄ N, per cent. .	56	27	31	15	30	21	33	17	24	22	23	16	5	16	..	4	40	46	34	19	26	46	51	..	40	46	33

was ingested and oxidized during the period of oatmeal diet. The fat in the gruel was very slightly greater than in the liberal diet, and as there was no evidence of acidosis before its use, it is not probable that the fat caused the change. The protein metabolism, however, is seen to undergo considerable variation. From a very high protein intake—higher than needed for the body use—there is a sudden drop,

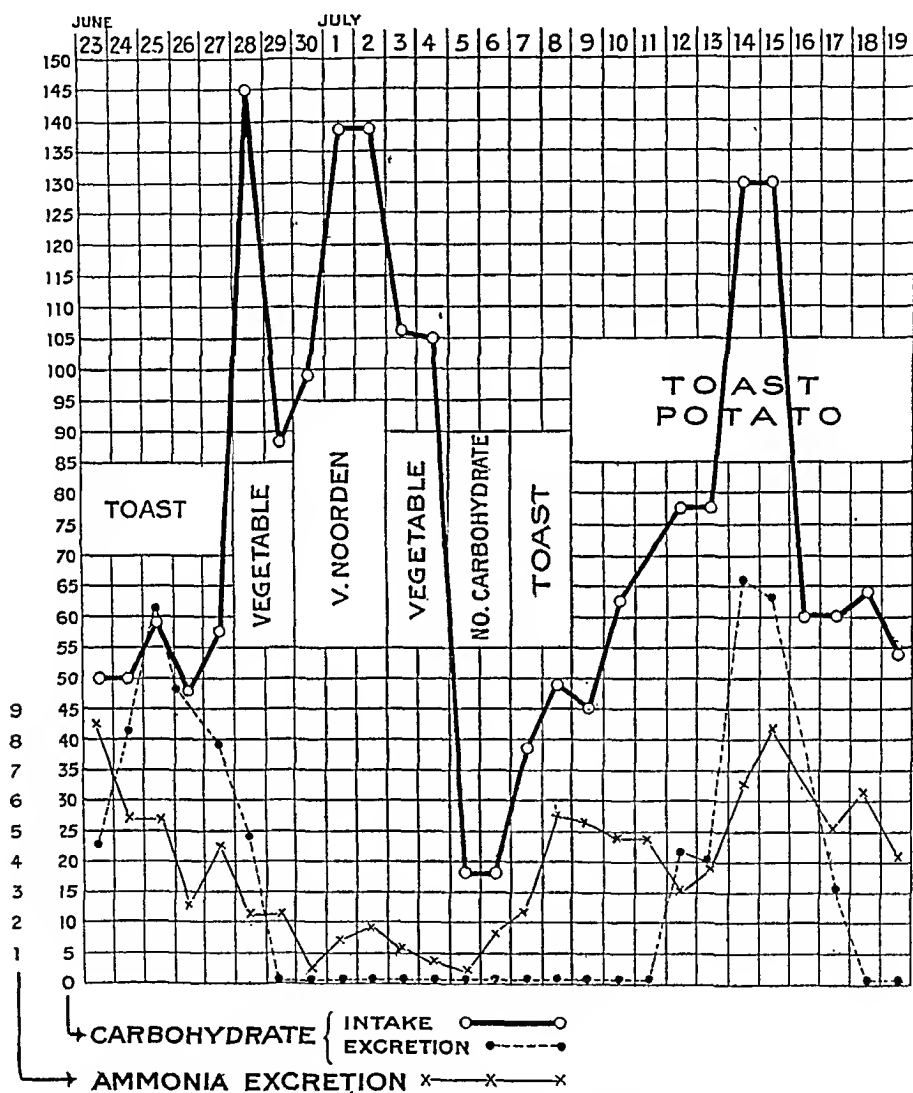


CHART II.—Case II. The second period, showing the increased carbohydrate tolerance and diminished ammonia excretion after a diet of vegetables and von Noorden's gruel.

and associated with this change in the food there is noticed a change in the nitrogen balance from plus to minus; that is evidence of the use of the patient's own tissues. Therefore, we conclude that an undoubted mild acidosis resulted when the gruel was used, but it was probably not due to the gruel *per se*, but to other factors in the regulation of the diet. However, we cannot exclude the possibility that

at this time the patient was not in a suitable condition to react properly to the von Noorden diet.

To study this point further, another series of observations was made later. On June 23, after the patient for two months had been allowed a diet restricted only in carbohydrates, he was placed on a standard test diet of known composition. This test diet was mainly to determine his capacity for oxidizing carbohydrate and of combating acidosis. At this time his general condition was unfavorable, the sugar elimination increased, and the signs of acidosis were marked. It will be seen from Table II and Chart II that he was using practically none of the carbohydrate in the food, and further, that a rather severe acidosis was present. The course of the dietary changes, with the urinary analyses from day to day, may be seen in detail in the table, and may be summarized in the statement that *the use of fresh vegetables and the von Noorden gruel resulted in raising strikingly the patient's tolerance for carbohydrates and in reducing considerably the degree of acidosis.*

It is also noted in Table II that there was a wide variation in the ammonia output, which diminished during the vegetable and oatmeal days and reached a higher point when the diet contained little or no carbohydrate.

In conclusion, it can be said that these two cases of traumatic diabetes ran a milder course than is usually seen in diabetes in children, but otherwise in their urinary and therapeutic reaction they did not differ essentially from cases of diabetes of non-traumatic origin.

BIOT'S BREATHING.

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IN 1876, Camille Biot¹ published a study of Cheyne-Stokes respiration, and in a postscript to the article he reproduces two pneumatographic tracings, taken from a boy, aged sixteen years, suffering from tuberculous meningitis, and comments upon these as follows: "Now these traces differ notably from those of Plate 1, Cheyne-Stokes breathing, especially in that before and after the pause there are no respiratory movements of a gradually increasing and diminishing sort, but instead a respiration which is

¹ Contribution a l'étude du phénomène respiratoire de Cheyne-Stokes, Lyon médical, 1876, xxiii, 517 and 561.

usually deep and dyspnoëic, corresponding to a deep sigh made by the patient at such times;" and later he adds: "Without wishing to draw definite conclusions from a single case, it seems, nevertheless, that in meningitis there exists not the true type of Cheyne-Stokes, but a type more or less related, more or less regular."

Two years later in a monograph² embodying further experimental and clinical study of Cheyne-Stokes breathing, he devotes a chapter to "*le rythme méningitique*." He quotes from a number of authoritative writers, among them Grisolle, Trousseau, and Jaccoud, to show that the characteristic respiration of meningitis, especially of the tuberculous variety, while irregular, and marked by periods of apnoea, is still quite unlike the Cheyne-Stokes type. The pauses occur at irregular intervals, and are often preceded or followed by a deep sigh. There are lacking the gradual diminution and increase in the force of the respiratory movements before and after the apnoëic periods. Shallow and deep, rapid and slow movements follow one another without any regularity or rule. He points out that the descriptions of both Cheyne and Stokes show that they had in mind a distinct and clean-cut clinical picture in which there is a regular succession of apnoëic pauses and of periods of breathing of gradually increasing and decreasing force, and he protests against the tendency to include under the term Cheyne-Stokes respiration a type presenting so many points of difference from that described by these two astute Dublin clinicians. Biot, therefore, did not and did not profess to describe a new variety of pathological breathing. He merely emphasized the salient features of a type of breathing which had long been noted as occurring in meningitis and other cerebral disturbances, and contrasted these with those of the type described by Cheyne and Stokes.

It is somewhat strange that in the abundant literature relating to Cheyne-Stokes breathing that has accumulated since the writings of Biot, so little consideration has been given to the type of breathing to which he called attention, and which since that time has usually borne his name.

Aside from the casual mention of it as a variety of Cheyne-Stokes breathing in a few works on diagnosis, it is rarely referred to. Hofbauer, in his careful pneumatographic study³ of the various types of dyspnoea, has evidently given the matter some attention, but his experience seems to have been unfortunate, for he dismisses the subject with the following words: "This form of breathing, so often described, I have never been able to find. Again and again when, upon simple inspection of the patient, I have thought that I had finally found a case of Biot's breathing, the graphic

² *Etude clinique et expérimentale sur la respiration de Cheyne-Stokes*, Paris, 1878.

³ *Semiologie und Differentialdiagnostik der verschiedenen Arten von Kurzatmigkeit auf Grund der Atemkurve*, Jena, 1904, p. 27.

representation has shown me that it was after all Cheyne-Stokes breathing."

As far as I have been able to discover, no graphic representation of this type of breathing has ever been published, other than the original tracings of Biot, which are here reproduced (Fig. 1). In each of these the descending limb of the trace records the inspiratory rise of the chest; the ascending limb, the expiratory fall.

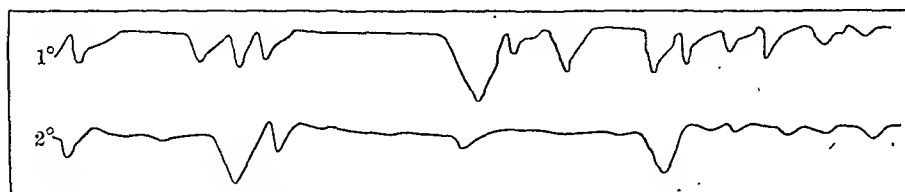


FIG. 1.—Copy of Biot's tracings illustrating the meningitic type of breathing. Down stroke = inspiration.

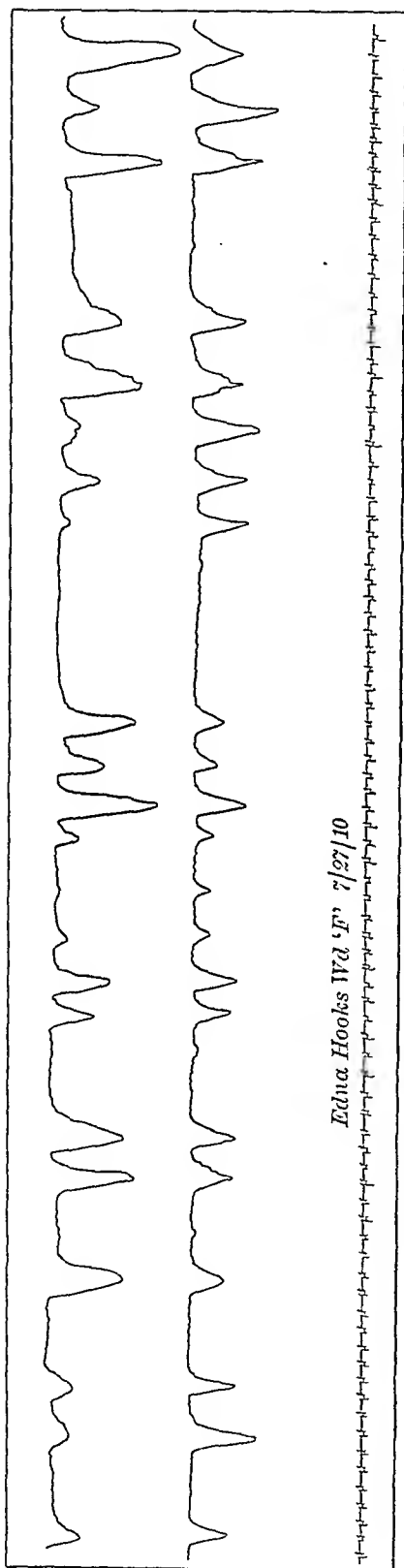
During the past two years, in the course of a more or less systematic graphic study of pathological types of breathing, I have encountered typical examples of Biot's type of respiration seven times. In six instances it occurred in the course of meningitis; in the seventh (Case VII), it was found in a child suffering from some intracranial complication of suppurative mastoiditis, the nature of which could not be determined.

The peculiarities of this type of respiration are well illustrated in the tracings shown in Figs. 2 and 3. The tracings obtained in all the other cases were in every respect similar to those here shown, so that it has not seemed worth while to reproduce tracings from every case.

The tracings were obtained by means of two pneumatographs of the Marey type, one placed about the thorax at the level of the third rib, to record the movements of the upper thorax; the other placed about the abdomen, midway between the ensiform and the umbilicus, to register the movements of the diaphragm. In each figure, the upper trace represents the movements of the thorax; the lower, those of the diaphragm. The descending limb of the trace indicates the inspiratory movement. The bottom line records the time in seconds.

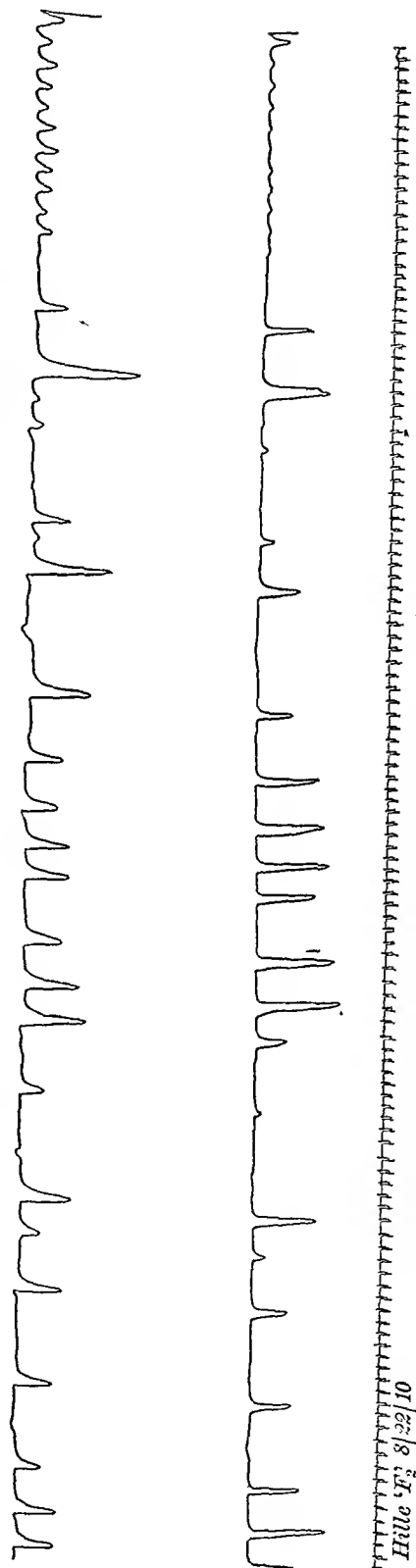
CHARACTERISTICS OF BIOT'S BREATHING. The characteristic features of this form of respiratory arrhythmia may be stated as follows:

1. Periods of apnoea, which vary in length and occur at irregular intervals.
2. Constant irregularity in rhythm, and in the force of the individual respirations.
3. The frequent occurrence of deep sighs.



Edna Hooks Wal. F. 7/27/10

FIG. 2.—Respiratory tracing from a case of tuberculous meningitis, showing Biot's breathing.



Hille F. 8/22/10

FIG. 3.—Respiratory tracing from a case of tuberculous meningitis, showing Biot's breathing.

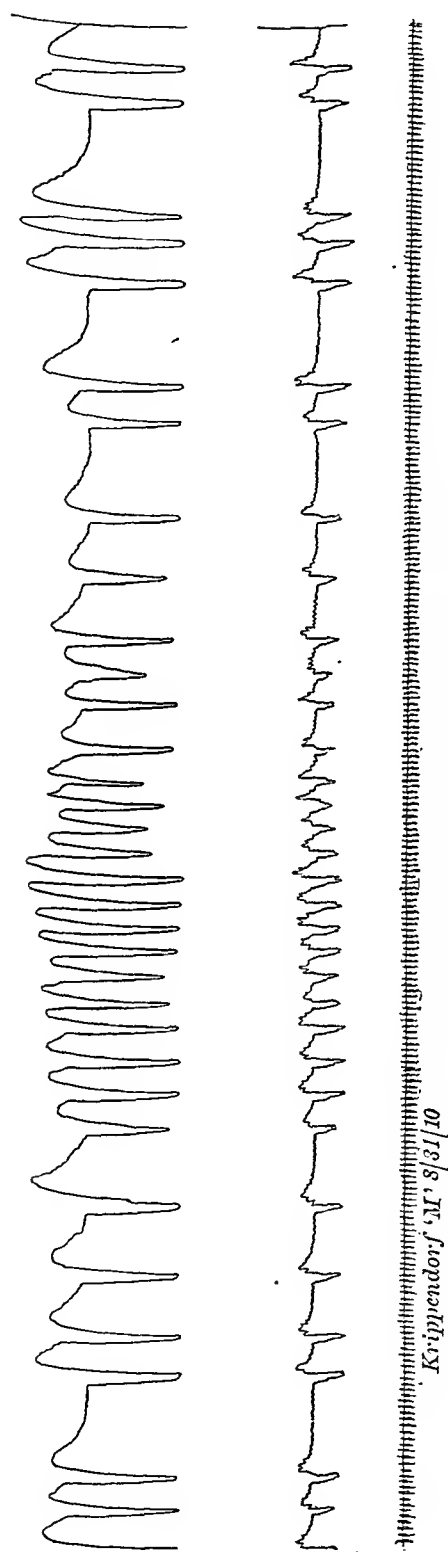


FIG. 4.—Respiratory tracing from a case of fatal anuria.

4. In addition to the above well-recognized features, I wish to mention one which in all of my tracings was so constant and striking as to seem to warrant its inclusion among the cardinal features of the condition. I refer to the great uniformity of the expiratory level. In spite of the constant variation in the depth of inspiration, the corresponding expiratory movement always carried the writing lever back to the same uniform level, so that the top of the trace formed a straight, horizontal line. This peculiarity seems to be due to the fact that the expiratory act is purely a passive one, and that the active, muscular expiration, so frequently seen in various types of respiratory disturbances, is altogether lacking.

This feature is well brought out by comparing the tracings of Figs. 2 and 3 with those of Fig. 4. These last were taken from a case of fatal anuria (Case VIII), the patient being in a condition of light stupor, and it will be seen that the ascending (expiratory) limb of the trace is always carried well above the mean expiratory level, as seen during the long pauses, and that the height of this expiratory rise varies with each respiration. These peculiarities are apparent in both the thoracic and the abdominal traces, and are the result of active, muscular expiratory efforts of both chest and abdomen.

This type of breathing corresponds in many respects with Biot's meningitic type: there are the apnœic pauses coming at irregular intervals, the constant variation in rhythm, and the constant, if slight, variation in amplitude. It differs, however, in the absence of the deep, sighing respirations, and especially in the markedly active character of the expiration; and I am inclined to believe that future study may show it to have a different pathogenesis, and justify its classification as a separate type of respiratory arrhythmia.

OCCURRENCE OF BIOT'S BREATHING. From the scanty information obtainable from the literature of the subject, it is evident that Biot's type of respiration has been supposed to occur not only in meningitis, but in other cerebral conditions as well. It is sometimes referred to as "cerebral breathing." No very definite statements upon this point, however, are to be found. Of the seven typical examples of this form of breathing among my own cases, 6 were proved to be cases of meningitis and the seventh (Case VII) may have been one, although this could not be proved. In the 24 other cases of meningitis studied, Biot's breathing was never detected. In other words, it was noticed in only about 20 per cent. of the cases observed.

In three instances it occurred in infants of two years or under; twice in children of eight years of age, and twice in adults. Of the 6 proved cases of meningitis 4 were of the tuberculous type, 1 was caused by *Streptococcus pyogenes* and 1 by *Diplococcus intracellularis*. Among a great variety of other diseases studied, including a number of cerebral conditions, such as hemor-

rhage, thrombosis, cerebral lues, etc., and various forms of coma, no instance of this type of breathing was found.

By referring to the condensed case reports it will be seen that when this type of breathing appeared it usually persisted through the greater part of the illness. In Case I it was observed almost daily through a period of five weeks. In four of the cases the irregularity was noticed upon admission to the hospital, only a few days after the onset of symptoms; so there can be no question that this respiratory arrhythmia may sometimes be an early, and therefore an important, sign of meningitis. Its occurrence seemed to bear no special relation to the state of the pulse (whether rapid, slow or irregular), or indeed to the presence or absence of any other symptom. It was seen in deep coma, and in states of consciousness in which slight drowsiness and apathy was the only departures from the normal.

RELATIONSHIP TO CHEYNE-STOKES BREATHING. Biot was quite warranted, it seems to me, in insisting upon the sharp distinction between this meningitic type and the form of breathing described by Cheyne and Stokes. The two types have really little in common. The dominant feature of Cheyne-Stokes breathing is the rhythmic succession of periods of apnoea and periods of dyspnoea. The apnoeic pauses in any given case are quite uniform in length and occur at regular intervals. The periods of dyspnoea are all composed of about the same number of respirations and show regularly a progressive waxing and waning in the force of the respirations. The characteristic feature of Biot's type on the other hand, is its complete lack of any sort of rhythm. The periods of apnoea vary in length and occur at irregular intervals and there is constant irregularity in both the rate and the force of the individual respirations. Such essentially different types of breathing must, it seems to me, have a different cause and pathogenesis. Among the cases here reported well-marked Cheyne-Stokes breathing was observed only once. In this case it replaced Biot's type during the last two or three days of life. In two other cases a slight suggestion of the Cheyne-Stokes rhythm was observed in the tracings on two or three occasions during the intervals when the breathing was, in other respects, normal. In Case I, in which tracings were taken almost daily over a period of five weeks, the Cheyne-Stokes type was never encountered. The fact that Cheyne-Stokes respiration is occasionally seen in patients who, at other times, show Biot's type only means, I think, that in such patients the intracranial conditions of—let us say—pressure or irritation are changing.

PATHOGENESIS. Concerning the pathogenesis of Biot's meningitic type of breathing there is little to say, since almost nothing is known. The only suggestion of an explanation that I have found is that ventured by G. A. Gibson⁴ in his comprehensive

⁴ Cheyne-Stokes Respiration, Edinburgh, 1892, p. 126.

historical and critical study of Cheyne-Stokes respiration. Accepting the conclusions of Marckwald that periodic breathing can only occur when some of the higher brain tracts have ceased to exert their influence upon the automatic centre in the medulla, he suggests that true Cheyne-Stokes breathing may require the total abolition of such higher brain influences and that the meningitic or cerebral type may result from "the irregular discharge of unequal impulses" from such higher tracts.

The inhibitory effect, upon respiration, of stimulation of the various sensory nerves is well known, and Marckwald⁵ has shown that this is preëminently true for the glossopharyngeal, which he refers to as "a true inhibitory nerve of respiration," coming into action, however, only under exceptional circumstances, as for example, during the inhibitory mechanism of swallowing. When this nerve is stimulated there is complete cessation of respiration for a short time and then breathing is resumed even though the stimulation of the nerve be continued. It has occurred to me that the peculiarities of Biot's breathing may possibly be explained by assuming an involvement of the root of the glossopharyngeal nerve in the meningitic inflammation, with resulting irritation of the nerve. This hypothesis is in line with the commonly accepted idea that many of the pulse irregularities of meningitis result from irritation of the vagus root. Thus far I have had no opportunity to examine, postmortem, the condition of the cranial nerve roots in cases which had shown this type of breathing. If such an hypothesis be correct we might reasonably expect to find Biot's breathing especially common in the epidemic type of meningitis, in which there seems to be an especial tendency toward involvement of the nerve roots. It was present in the only case of that form of meningitis that I have had an opportunity to study graphically.

A synopsis of the histories of the cases which form the basis of this paper is as follows:

CASE I.—Man, aged thirty-eight years. No. 18,798. Admitted to the hospital September 18, 1909; died November 13, 1909. Eight days before, while in good health, he had undergone some operation upon the nose and a few hours later had developed backache, headache, fever, and vomiting. Since then fever, severe headache, and increasing stupor. On admission stupor, rigidity and tenderness of neck, unequal pupils and paresis of right side of face and right arm and leg. The turbid spinal fluid, obtained on several occasions, always yielded a pure growth of *Streptococcus pyogenes*.

The disease ran a subacute course with periods of marked remission in the symptoms. Much of the time the patient was

⁵ The Movements of Respiration, London, 1888, p. 90.

conscious and fairly comfortable. Distinct irregularity of the breathing was first noted on October 9, and was present most of the time up to his death on November 13. The heart action remained regular to the end. A pronounced diuresis was noted through the greater part of the illness. Two days before death he developed a right-sided pneumothorax, presumably as a result of an aspiration pneumonia, but even after this the breathing retained its characteristic irregularity. Many pneumatographic tracings were taken between October 9 and November 13. Most of these presented all the characteristic features of Biot's breathing, that is, variations in rhythm and force, occasional deep sighing respirations, and periods of apnoea varying in length and occurring at irregular intervals. Occasionally during periods of temporary improvement, the breathing would be quite normal. At no time was the respiration of the Cheyne-Stokes type.

CASE II.—Girl, aged eight years. No. 20,072. Admitted July 15; died August 3, 1910. Illness began four days before admission, with headache which grew very severe. Later vomiting, fever, drowsiness, nocturnal delirium, rigidity of the neck, slight Kernig's sign, strabismus, coma, and death on November 3. Tubercle bacilli were found in the spinal fluid. Respiratory irregularity was first noted on July 23.

On July 26, 27, and 28, tracings showed typical Biot's breathing (Fig. 2). July 29, breathing much more rapid and more regular, but tracings show short periods of apnoea and some variation in rhythm and force. July 30, tracings are suggestive of infantile type of Cheyne-Stokes. July 31, typical Biot's breathing.

August 1. Tracings suggestive of Cheyne-Stokes.

August 2. Breathing rapid and almost regular in rhythm and force.

August 3. (Moribund) breathing very rapid and regular.

CASE III.—Male child, aged fourteen months. No. 20,267. Admitted August 18; died August 27, 1910. Illness began abruptly five days before admission, with general convulsions, vomiting, diarrhoea, and fever. Later drowsiness, stiff neck, retraction of head, stupor, and ultimately coma. Tubercle bacilli were found in spinal fluid. On admission it was found that the respiration was irregular in rhythm and depth and showed long apnoeic pauses.

August 22. Tracings showed typical Biot's breathing (Fig. 3).

August 23. Breathing rapid and fairly regular most of time.

August 24. Tracings suggestive of Biot's type, but with no deep sighs and no long pauses.

August 25 and 26. Tracings similar to those of August 24.

August 27. (Moribund) breathing very rapid and almost perfectly regular.

CASE IV.—Male child, aged twenty-one months. No. 20,337. Admitted August 31; died September 10, 1910. Well up to six days before admission; then developed alternating drowsiness

and restlessness. Later fever, twitching of limbs and head, and rolling of eyes. On admission the child was stuporous, the neck was slightly stiff, eyes constantly moving from side to side. Well-marked bilateral Kernig's sign. Respiration was "shallow and irregular, with no long pauses." On September 2, several general convulsions. Comatose during last few days of life.

The spinal fluid was clear and sterile on culture. Examinations for tubercle bacilli were negative, but fluid injected into a guinea-pig resulted in tuberculosis to the animal. Tracings taken every day between September 1 and 6, showed typical Biot's breathing each time. On September 7 and 8, however, the tracings showed distinct Cheyne-Stokes breathing of the infantile type.

CASE V.—Boy, aged eight years. No. 20,708. Admitted November 10; died November 25, 1910. One month before admission a large, red, and tender swelling appeared in left axilla which was opened and discharged pus. Two weeks later illness began with persistent frontal headache. Four days before admission went to bed and has since had headache, fever, restlessness, twitching of hands, rolling of eyes, and nocturnal delirium. On admission neck stiff and tender; marked bilateral Kernig's sign; conjugate deviation of eyes. Breathing was irregular, with long periods of apnoea. During last few days of life, stupor deepening into coma. Tubercle bacilli found in spinal fluid. During the first two days the twitchings of limbs and body were so constant as to make it impossible to obtain satisfactory tracings of the respiratory movements. After that the tracings usually showed distinctly Biot's type of irregularity. Occasionally the breathing would be almost perfectly regular; occasionally, too, the tracing would show a tendency to the Cheyne-Stokes type. During the last two days of life the respirations were very rapid and regular.

CASE VI.—Colored woman, aged nineteen years. No. 20,887. Admitted December 16, 1910. In good health up to time of present illness. Sudden onset one week before admission, with severe headache and backache. Headache constant day and night. For past two days has been delirious, has had stiffness of neck and has vomited frequently. On admission, patient had high fever, stiffness, and tenderness of neck, retraction of head, unequal pupils. The breathing was irregular in depth and rate, and showed long apnoeic pauses. Pulse rapid and somewhat irregular. The cloudy spinal fluid was under high pressure and was increased in amount. It contained an increased number of both mononuclear and polynuclear cells. Smears showed a few Gram-negative intracellular diplococci, but no growth was obtained in the cultures. The severe symptoms persisted for several days, and then gradually subsided, the convalescence being complicated by an attack of erysipelas. Tracings taken on December 20 and 21 showed typical Biot's breathing.

CASE VII.—Female child, aged two years. No. 20,719. Admitted November 14, 1910. Discharge from left ear since an attack of measles some months before. Illness began four days before admission, with fever and vomiting. Has been listless and apathetic, restless at night, and has vomited frequently. On admission child was dull, the pupils were equal and reacted normally. No stiffness nor tenderness of neck, no paralysis, normal reflexes, no Kernig's sign. Temperature, 99 to 101. On November 18 patient had become stuporous, right pupil larger than left, paralysis of left facial nerve, tenderness over mastoid region, slight papillitis of both eyes. Tracings showed well-marked Biot's breathing. Examination of spinal fluid negative. The child was operated upon, and a suppurative mastoiditis found. No thrombosis of lateral sinus. Exploration failed to reveal a brain abscess. Death; no autopsy.

CASE VIII.—Married woman, aged twenty-nine years. No. 40,593. (Service of Dr. Bolton.) Admitted August 16; died September 3, 1910. For two years pain in left loin, with bloody urine. For three months has been passing "gravel" in urine. On August 22, operation on left kidney; several calculi found in pelvis; kidney removed. From then until the time of her death thirteen days later, the patient had practically complete anuria. She grew stuporous and finally comatose. Vomiting was persistent. Pulse slow and feeble. Blood pressure low. The respirations were slow and irregular and showed very marked active expiration. Tracings taken on several occasions always presented the same characteristic form (Fig. 4). An autopsy showed extensive cystic degeneration of the remaining kidney.

It is my pleasant duty to acknowledge my obligation, and to express my thanks, to Dr. R. G. Stillman for the very material help rendered by him in the work whose results are here recorded.

THE MYOGENIC DOCTRINE OF THE CARDIAC ACTIVITY AND ITS RELATION TO ARRHYTHMIA.

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No portion of cardiac physiology and pathology has excited more interest and controversy than has the subject of arrhythmia or irregularity of the heart. Although most types of arrhythmia

have long been recognized clinically, their true physiological significance and proper interpretation has been the result of a comparatively recent revolution in our views of the cardiac function. It may, therefore, be of some interest to take up certain of the more usual forms of cardiac irregularity from the standpoint of the modern physiology of the heart.

Before entering upon a discussion of the several forms of arrhythmia it will be of advantage to briefly consider certain facts in the physiology of the heart which are essential to a proper understanding of cardiac irregularity.

Scarcely more than a decade has elapsed since it was quite generally taught that the cardiac contraction was the result of a nerve impulse generated within the nervous system and conveyed to the heart muscle cells, the mechanism of which was not unlike that of voluntary skeletal muscle. Through the minute and painstaking physiological researches of Gaskell, Bowditch, especially of Engelmann, and others, this so-called neurogenic origin of the heart action was called into question and the view was advanced that the contraction stimulus develops within the cardiac muscle cell itself and is not dependent upon outside nervous agencies. This latter view has been called the myogenic doctrine, and with its advent the modern era of cardiac physiology may be said to have begun. It would be beyond the province of this paper to attempt to discuss the relative merits of the neurogenic and myogenic theories of the heart's contractions, concerning which so much dispute has arisen among the most eminent physiologists and clinicians. Suffice it to say, that, although today the question is far from being definitely settled, nevertheless, the weight of reliable embryological, anatomical, and physiological evidence tends largely to support the myogenic doctrine. It may be, as is suggested by Mackenzie, that the truth lies midway between these two opposing doctrines which may ultimately be reconciled. It is undeniable that in the fully developed mammalian heart there exists a complex nervous mechanism inseparably associated with the cardiac musculature. For this reason the writer hazards the belief that, although the chief seat of the cardiac stimulus is to be found within the muscle cells, the nervous system is employed by nature, in the heart, as is some of the secretory glands, as a "factory of safety." Certain glands will continue to secrete when entirely removed from all nerve influence, because of stimulation derived from chemical substances supplied from other glands. So, with the heart, it is possible that there are two modes by which cardiac action is maintained—either through the nervous system or through the heart muscle itself—and that this dual relationship affords a valuable factor of safety.

Briefly stated the myogenic theory assumes that the heart is an automatic organ, as it were, in which the stimulus that causes the contraction is generated within the heart muscle cells and is not

conveyed to them by the nervous system. Moreover, this contraction stimulus is not conducted to the various portions of the heart by means of nerve fibers, but is carried progressively onward by the muscle fibers themselves: thus causing the wake-like contraction of the heart which begins at the base and is propagated through auricles and ventricles toward the apex. Furthermore, it has been shown that the cardiac muscle cells possess in addition the properties of contractility, irritability and tonicity. Although the coöperation of these fundamental functions is sufficient to enable the heart to carry on its rhythmic contractions, the adjustment of the cardiac activity to the widely varying needs of the body in the higher mammals at least, is controlled and regulated by a complex extra- and intra-cardiac nervous mechanism, impulses from which are capable of inhibiting or stimulating any or all of these functions of the muscle cells.

We see, therefore, that the cardiac muscle is endowed with five so-called cardinal properties, namely:

1. *Stimulus Production.* The power of producing a stimulus which can cause the heart to contract.

2. *Excitability.* The property of receiving and responding to a stimulus.

3. *Conductivity.* The ability to propagate a stimulus onward from fiber to fiber.

4. *Contractility.* The power of responding by contracting when stimulated.

5. *Tonicity.* The property by which muscle maintains a certain degree of contraction even when inactive.

For a moment let us consider these functions in more detail. It is assumed, according to the myogenic doctrine, that the heart muscle cells inherently possess the power of originating stimuli which are capable of causing the muscle fibers to contract, *stimulus production*. The stimulating material originating within the cells, results from chemical activity largely dependent upon the action of inorganic salts of the blood serum. Ringer and Howell hold that calcium plays the important role in producing cardiac contraction, whereas Loeb maintains that sodium furnishes the chief motive power. In any event, it seems likely that the muscle cells elaborate a substance which is stored up during the diastole of the heart and when a sufficient quantity has accumulated the heart is stimulated to contract. At each contraction the entire supply of stimulus is exhausted, only to be reaccumulated during the next period of rest.

Since a heart contracts when stimulated, there must obviously be stored up within the muscle cells energy. In order that a stimulus may produce a contraction the muscle cells possess the property of transforming the stimulus into movement, this liberating energy. This property of responding to a stimulus is termed *excitability*.

It has been shown that not only do the cardiac muscle cells originate stimuli, but they are also capable of transmitting a stimulus from muscle fiber to muscle fiber without the aid of nerves, in short they possess *conductivity*. In proof of this it has been demonstrated by Englemann that by artificial stimulation a contraction wave may be induced in any part of the heart muscle. Indeed, he showed that a heart can be artificially made to contract in a direction diametrically opposite to the normal. Furthermore, he found that when an irregular piece of the ventricular muscle is cut in such a way as to sever all possible nerve connections and yet leave some of the muscle cells in continuity with each other, such a portion of the muscle conducted impulses quite as well as did a straight strip of cardiac muscle. Moreover, the slow rate at which impulses are conducted by the heart muscle is an additional argument against the nerve paths playing any part in the conduction of stimuli.

Little need be added in explanation of the ability of the normal heart muscle to contract, since *contractility* is the most obvious function of all muscle tissue when stimulated.

Like other muscles the heart also possesses the ability to maintain a certain tone, that is, its muscle fibers under normal conditions maintain a certain tension and do not relax to their full extent even during diastole. The importance of *tonicity* is made manifest when we consider that some of the most noteworthy features of heart failure are the result of a deficiency of this function.

A striking peculiarity of heart muscle which should be mentioned is that when a heart contracts, due to the exercise of its five cardinal properties, all these properties are for the time entirely destroyed, returning gradually during the period of rest which ensues. Because of this there is a time in each cardiac cycle during which the heart muscle fails to be excited to contract, no matter what the stimulus. This period was termed by Marey, its discoverer, the "refractory phase" of heart muscle. It has been found that in a rhythmically beating heart the refractory phase begins just before systole and continues until a short time after it. During systole, therefore, a heart is not excitable, but after systole ends the conductivity, excitability, and contractility are gradually restored to the muscle fibers at the same time that the stimulus producing material is being reaccumulated. Finally, when a sufficient quantity of stimulus has been elaborated, the other functions have so far recovered themselves as to respond to the stimulus, thus giving rise to a new systole. The longer the diastole the greater is the excitability, contractility, and conductivity, of the heart muscles, the weaker is the stimulus necessary to cause a contraction, and the greater is the resulting contraction. The significance of the refractory phase will be more clearly appreciated when we discuss the subject of extra systoles.

A second characteristic of the cardiac musculature was discovered by Bowditch and is known as the law of "maximal contraction." He showed that when a heart responds to a contraction stimulus, it contracts with all the force which it is capable of exerting at that moment. The size of the contraction bears no relation to the strength of the stimulus, a powerful stimulus cannot produce a greater contraction than a weak one. In short, when a heart is stimulated it either contracts with its maximal power or not at all.

In the primitive cardiac tube of certain embryos, it is clearly seen that the contractions begin at the venous end and sweeping forward toward the arterial end involve successively in a peristaltic wave, first the sinus venosus, then the auricle, the ventricle, and lastly, the aortic bulb. It is at the sinus, therefore, that the primary stimulus is produced, the sinus initiates the cardiac rhythm and becomes, as Erlanger says, "the pace-maker of the heart." In the higher animals and man, the structure of the heart becomes more complicated. The sinus is no longer found as an independent chamber, but becomes merged within the auricle, which, like the ventricle, is ultimately subdivided into two chambers, forming the right and left side of the heart, while the aortic bulb becomes part of the ventricle.

Recent investigations have shown that within the adult human heart there persist definite groups of muscle cells which are the remains of the embryonic cardiac tube and which it is reasonable to assume retain their primitive power of originating contractions and of conducting them. Keith and Flack have demonstrated remains of the sinus venosus connecting the great veins with the auricle. This node of muscle tissue they called the sino-auricular node. At this point it is believed that the normal stimulus of the human heart originates and from here the contractions start. From the sino-auricular node the impulse travels through the auricular walls toward the ventricle, causing the auricular contractions. His, Jr., Tawara, Kent and others have demonstrated a bundle of primitive muscle fiber which begins in the auricular wall near the opening of the coronary sinus as the auriculo-ventricular node. From this node fibers pass down in the membranous septum, forming the auriculo-ventricular bundle, or so-called Bundle of His, until they reach the muscular septum which they straddle by dividing into two branches, one group passing to the right and the other to the left ventricle, thus, roughly speaking, forming an inverted Y, the stem of which projects up into the right auricle along the auriculo-ventricular walls. In the ventricle these muscle bundles split up into numerous ramifying branches. Down this auriculo-ventricular bundle the cardiac impulse is propagated from auricle to ventricle and it is probable that this bundle forms the most important if not the only conduction path between these chambers.

From the above consideration of certain facts in the physiology and anatomy of the heart it may be readily seen that aside from its interest to the physiologist and morphologist, the myogenic doctrine has come to be of wide significance to the clinician. Through its clinical application many of the most baffling features of heart diseases have been rendered intelligible and much that was shrouded in the gloom of speculation and uncertainty has been brought forth into the clear light of demonstrable fact. Certainly no phase of heart disease has been so profoundly altered and modified by the gradual acceptance of the myogenic doctrine as has been the study of that extremely important phenomenon of cardiac pathology—arrhythmia.

Of late years advances in medicine have been marked by the constant introduction of the more exact methods of study. For the study of the cardiovascular system there have been devised many instruments of precision. Foremost among these in importance stand the various forms of cardio-sphygmographs, instruments by which we are enabled to obtain simultaneously graphic records of the movements of the radial artery, apex beat, and jugular pulse. By means of tracings taken at these positions we obtain with surprising accuracy a conception of the events which are taking place on both the right and left sides of the heart. The waves obtained from tracings of the pulse in the jugular vein, the venous pulse, show the movements of the right auricle, whereas the movements of the left ventricle are indicated by the radial and apex tracings. It is beyond the scope of these remarks to enter into a discussion of the technique of these methods of investigation. It should merely be pointed out that the satisfactory analysis of any form of cardiac irregularity can only be accomplished by a study of such tracings. The forms of cardiac irregularity which shall take up where studied in this way. For the sake of clearness actual tracings will not be used to illustrate these irregularities, but instead a series of diagrams based upon tracings. For these diagrams I am indebted to an article published recently by K. F. Wenckebach, a worker whose tireless energy and masterly researches in the field of cardiac pathologic physiology have added so much to our knowledge of arrhythmia.

In these diagrams the abscissas represent the time, the horizontal lines, the subdivisions of the heart, that is, sinus, auricle, and ventricle. The perpendiculars in the upper row indicate the contractions of the sinus venosus found at the venous ostia where the stimulus originates, the middle row of lines represents the auricular contractions, while the lowest row indicates the ventricular movements. The number 20 has been arbitrarily adopted as the number of time units required for a cardiac revolution. In other words, at the venous ostia it requires 20 units of time for stimulus production, contractility and conductivity to reach

the point at which they are capable of initiating a new cardiac contraction.

Arrhythmia has been variously divided, the number of classifications differing almost with every author writing upon the subject. Among the clearest and most satisfactory classification is that adopted by Wenckebach. He classifies irregularity of cardiac action into two great groups. To the first group he gives the name true arrhythmia, because the fundamental sinus rhythm of the heart is disturbed. To the second he applied the term pararrhythmia. In this latter group the fundamental rhythm has not ceased to exist, although various influences obscure it from time to time. The term allorhythmia is frequently met with especially among French writers, but Wenckebach maintains that its use should be restricted to the particular class of pararrhythmias in which the irregularities manifest a certain periodicity and recur regularly. (Example—the regularly intermittent pulse of disturbed conductivity.)

The first group need not detain us long. True arrhythmia, or as it has been called by Mackenzie, sinus irregularity, results when stimuli are produced at the sinus rests at varying intervals instead of at regular intervals as is normal. The result of this irregularity in the rate of stimulus production shows itself in tracings chiefly as a variation in the length of diastole, the systolic phase of the cardiac cycle remaining practically constant. The rate of the pulse is temporarily altered by the variations in the length of the diastole, the auricle and ventricle being subject to the same influence show identical variations in their rate of contraction.

In the human heart the rate at which stimuli are discharged is largely governed by the accelerator and inhibitory nervous mechanism. It is, therefore, not surprising that we find true arrhythmia frequently associated with disturbances of the nervous system, as in meningitis. Respiratory irregularities fall under the head of sinus irregularity, as does the reflex effect of swallowing upon the heart-rate. The irregularity so frequently encountered in children with apparently normal cardio-vascular systems, the juvenile arrhythmia of Mackenzie, has been shown to belong to this group. Serious symptoms referable to the heart either objective or subjective, are rarely associated with sinus irregularities to which in themselves but little clinical importance need be attached.

On the other hand, the second group, the pararrhythmias offer greater difficulties in recognition and are of vastly more importance clinically. We will therefore, direct our attention chiefly to a study of the best understood forms of pararrhythmia. These include irregularity of the heart due to, first, extra systole, which may be auricular, ventricular or auriculo-ventricular; second, impairment of conductivity, that is, partial or complete heart block; third, depressed excitability; fourth, disturbed contractility, and fifth, so-called arrhythmia perpetua or absolute irregularity.

The most frequent form of pararrhythmia is the extra systole. Mackenzie has defined an extra systole as a premature contraction of auricle, ventricle or both in response to a stimulus produced at some abnormal point of the heart, but where otherwise the fundamental or sinus rhythm of the heart is maintained. For example, if in a rhythmically contracting heart we suddenly interrupt diastole by stimulating mechanically or electrically some portion of the auricular or ventricular musculature in such a way as to cause a premature additional contraction of the heart we produce experimentally an extra systole. It is perhaps confusing to refer to extra systole as premature contractions, since, strictly speaking, an extra systole is not a precocious contraction, but is a supplementary superadded contraction.

The effect of an extra systole is readily observed in the radial pulse where it produces a small pulse-wave, scarcely perceptible to the finger, which is followed, usually, by an abnormally long pause. This pause in the pulse conveys the impression that a beat is missed, hence, such a pulse is often spoken of as an intermittent pulse. It may be that the extra systolic contractions are so feeble that the resulting pulse-wave never reaches the radial. Palpitation of the pulse in such a case would lead one to think that a heart-beat had been missed, but auscultation of the heart or a tracing of the apex beat taken while the radial pulse is being examined will show that such is not the case and that during the apparent intermission a feeble contraction of the heart has actually occurred.

Extra systoles may vary widely in the frequency of their occurrence. Several may follow each other in rapid succession, they may recur regularly after a definite number of normal beats, or their reappearance may be absolutely irregular. In any event, it will always be seen that during the time the circulation is free from this disturbing influence the pulse is regular, because the fundamental or sinus rhythm of the heart has not been in any way altered.

As yet a positive explanation for the occurrence of extra systole is wanting. Mackenzie has advanced the view that extra systoles result from stimuli originating within muscle fibers which are the remains of the primitive cardiac tube, other than those found near the mouth of the great veins. He argues that since the normal rhythm starts in the sinus—remains at the veins, why should not the primitive muscle cells composing the auriculo-ventricular node and bundle of His, if for some reason rendered abnormally excitable, be capable of starting these extra contractions.

Just what agency is responsible for the extra stimuli is not known. By some it has been held to be an external excitant, as a toxine, which acts upon the heart much as experimental mechanical stimuli do. It is far more probable, however, that extra systoles are the

result of some autochthonous stimulus produced within the heart itself.

The variety of extra systole most often encountered is the ventricular form (Fig. 1 *a*). The mechanism of a ventricular extra systole is as follows. Within the ventricular wall there is generated the abnormal extra stimulus which suddenly interrupts the normal diastole of the ventricles by causing a contraction. This abnormal contraction is an extra systole and is followed by a long interval of rest. You will observe in Fig. 1 *a* the length of the pause following the extra systole exactly compensates for the precocity of the extra contraction and is known as the "compensating pause." The length of the compensating pause varies with the part of diastole in which the extra systole occurs, the later in diastole the extra systole takes place the shorter is the compensating period rest. The explanation for this compensating pause has been alluded to while discussing the refractory phase of heart muscle. Because of the extra contraction, the conductivity, contractility and excitability of the ventricular muscle has been entirely

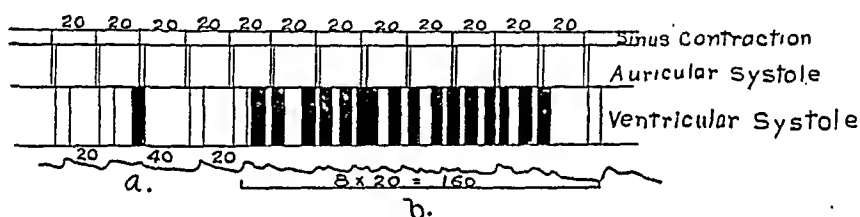


FIG. 1.—Ventricular extra systoles. In all the diagrams the shaded perpendiculars indicate abnormal contractions.

exhausted, the muscle has become refractory, hence the motor impulse brought by the next normal auricular contraction fails to arouse any response from the ventricle, and the pause therefore ensues. During the period of quiescence the ventricular muscle has an opportunity to regain its cardinal properties, hence the next auricular contraction reaches a readily excitable ventricle which responds normally and continues to do so until another extra systole interferes. In the simplest type of ventricular extra systole the compensating pause is complete and the time intervening between the end of the last normal contraction preceding the extra systole and the first one following it, equals exactly the time of two normal cardiac cycles. In Fig. 1 *a* the normal cardiac rhythm is 20 units of time and the period during which the extra systole occurs equals double that or 40 units of time. The abortive pulse wave in the radial which is caused by the extra systole is indicated in the radial tracing at "a." It will be noticed that the fundamental rhythm of the heart is undisturbed and that the auricles contract regularly and normally. It may occur as in Fig. 1 *b* that a number of entricular extra systoles succeed each other in rapid succession in

which case several normal ventricular contractions are replaced. When a considerable number of extra systoles follow each other it will still be found that the duration of the irregular period corresponds to a multiple of the time required for a normal cardiac cycle. (Ex. 8 cycles = $20 \times 8 = 160$: Fig. 1 *b*.)

In connection with ventricular extra systoles the subject of the so-called *pulsus bigeminus* may be mentioned. As has been said, extra systoles may recur regularly after every 1, 2, 3, or 4 normal contractions. When the extra contractions follow after every normal beat there results a pulse tracing in which two closely connected beats are followed by a long pause and again two more beats, etc. Because of the paired character of the pulse-waves, such a pulse has been erroneously termed a *pulsus bigeminus*. The expression is a misnomer, for, as Wenckebach contends, far from being twins the two contractions are of totally different origin, the first being a normal contraction and the second an extra systole. Whether or not that true bigemini of the pulse, in the sense that Traube originally meant it, ever occurs is doubtful, unquestionably the vast majority of cases of bigeminal pulse are the result of extra systoles following every normal contraction.

More rarely it happens that extra systole take their origin from the auriculo-ventricular node. These are called nodal extra systoles. In this event the abnormal stimulus arising midway between auricle and ventricle propagates a contraction wave simultaneously up and down. Hence the auricle and ventricle contract prematurely and together. The abnormal motor wave traveling back through the auricle reaches the sinus, there it destroys the normal stimulus material which has been accumulating so that a normal interval results before the sinus is again able to initiate a cardiac contraction. Therefore, in nodal extra systoles the compensatory pause is too short, that is, incomplete, as is seen in Fig. 2 at *a*, the compensatory pause being 37 instead of 40.

A third variety of extra systole is shown in Fig. 3 *a*. Here the extra systole begins in the auricle causing a premature auricular beat which is followed by a ventricular systole in normal order. A retrograde wave from the auricle in these cases is alleged to effect the sinus. Like ventricular extra systoles, the auricular ones are also followed by a compensatory pause, but the refractory phase of the heart ends sooner and the compensatory pause is again incomplete. (In Fig. 3 *a* it is only 34 instead of 40 as in the case of the ventricular extra systole.) But in all these forms of extra systole it will be seen that the heart invariably returns to its normal fundamental rhythm.

A fourth form of extra systole is described which is supposed to originate at the remains of the sinus venosus about the mouth of the great veins. However, the three main varieties which have been dealt with in some detail will serve to illustrate this extremely

common and important form of arrhythmia which results from alterations in the cardinal property of stimulus production and possibly irritability.

A second interesting type of pararrhythmia is associated with disturbances of the fundamental function of conductivity. We have discussed how the contraction wave sweeps down the heart from sinus to ventricle as it is conducted through certain groups

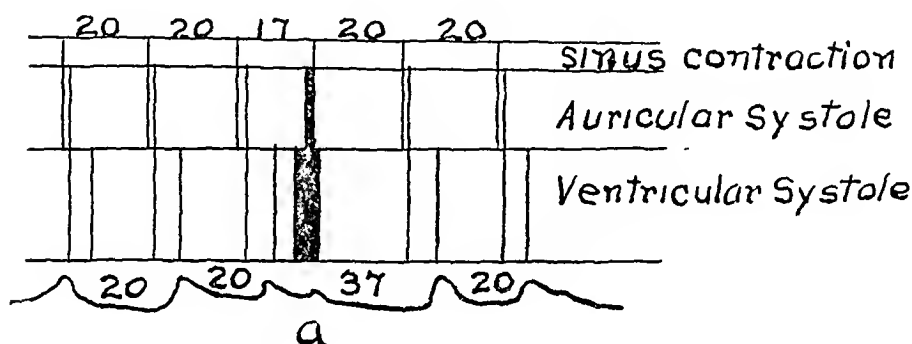


FIG. 2.—Auriculo-ventricular or nodal extra systoles (a.)

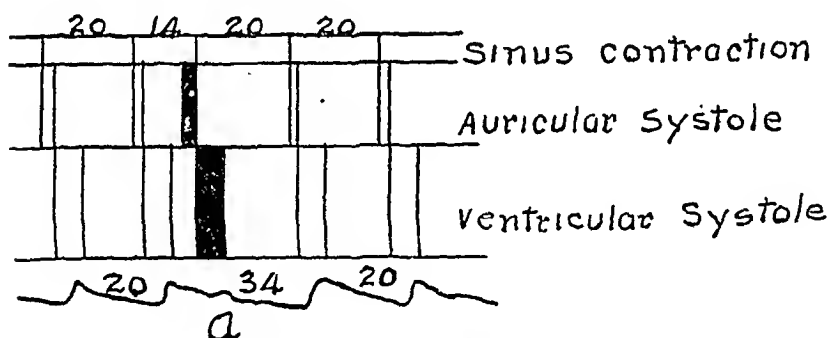


FIG. 3.—Auricular extra systole.

of the cardiac muscle cells and how after each systole of the heart this conductivity is temporarily suspended. When for any reason the power of the heart cells, to conduct stimuli, is depressed, a characteristic irregularity results, due to the fact that the diseased heart muscle regains its power of conductivity after a contraction more slowly than normal. The chief seat of diminished conductivity is the auriculo-ventricular bundle.

For example, as in Fig. 4, after a regular cardiac contraction, the conductivity being depressed, recovers slower than the other functions. Therefore, when the next contraction stimulus arises it finds the conduction power of the muscle cells not fully restored, hence the contraction wave traverses the heart more slowly than normal; that is, the time intervening between the auricular and ventricular systoles, the *a-v* interval, is longer than the normal

one-fifth of a second. This delays the ventricular systole so that the next stimulus finds the conductivity still more depressed and the third ventricular systole follows the auricular systole at even a longer interval that did the second. Finally the fourth contraction wave sweeps down the auricle, encounters muscle cells devoid of all power of conduction, the impulse is not transmitted therefore to the ventricle, which fails to contract at all, and a beat drops out. The failure of the ventricle to contract gives the heart muscle a sufficiently long rest to allow conductivity to be restored once more so that the next stimulus finds it responsive and a normal contraction results in which the ventricle contracts immediately after the auricle. Again conductivity begins to fail and after a certain number of beats the ventricle once more is quiet. This phenomenon may recur at regular intervals for an indefinite time and furnishes the best example of a regularly recurring irregularity or *allorhythmia*. As was stated, the seat of such disturbed conductivity is practically always the auriculo-ventricular bundle and the condition is one of incomplete heart block.

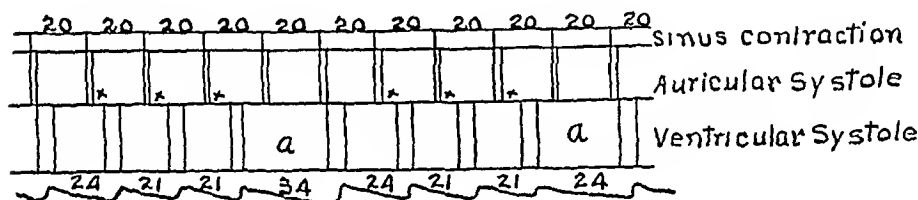


FIG. 4.—Impaired conductivity (incomplete heart block). Note at (x) the increasing interval between the end of the auricular and the beginning of the ventricular contractions, until finally at (a) a ventricular contraction completely drops out.

When the depression of conductivity reaches a high grade a ventricular systole may drop out after every third, second, or even after each beat. The most striking condition is observed in those cases in which, because of anatomical lesions, such as sclerosis or gummata of the bundle of His (auriculo-ventricular bundle) there is a break in the continuity of the conduction path between the auricle and ventricle. The contraction stimulus in such cases is blocked in the auriculo-ventricular bundle so that the ventricle is entirely cut off from the normal sinus stimulation. The result is the condition of complete heart block. Instead of ceasing to beat, as might be supposed, the ventricle after some irregularity initiates an independent rhythm of its own, because like other portions of the heart it possesses the power of "rhythmicity." The auricle, on the other hand, continues to follow the sinus rhythm. There results complete disassociation of auricle and ventricle, each following an independent rhythm as is seen in Fig. 5.

Clinically, cases of complete heart block may be recognized by the extremely slow radial pulse, usually 30 or under, while the

venous pulse in the neck, representing the movements of the right auricle may be seen to be beating, 2, 3, or 4 times as fast. They are usually associated with nervous phenomena as syncope, convulsions, etc., pallor, and respiratory disturbance, the whole condition giving rise to the symptom complex called Stokes-Adams syndrome.

Disturbances of conductivity, it is said, may also occur between the sinus rests and the auricle at the sino-auricular junction.

Lack of the cardinal function of excitability has also been described as producing irregularity. Pararrhythmia from this cause is certainly rare and is extremely difficult of analysis, in fact, its recognition seems to largely depend upon exclusion.

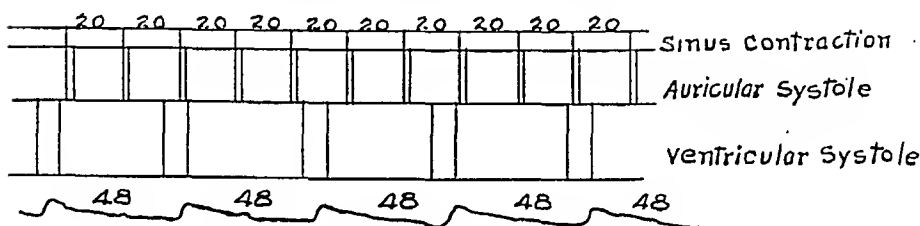


FIG. 5.—Complete disassociation between auricular and ventricular contractions (complete heart block).

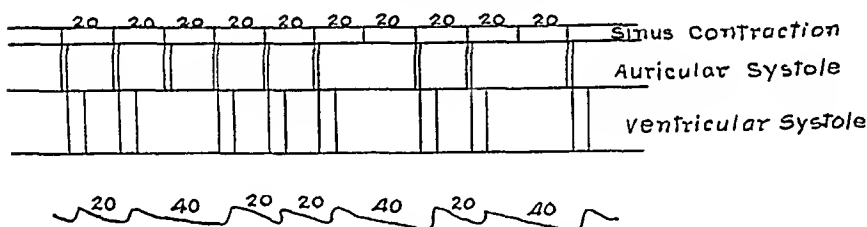


FIG. 6.—Impairment of excitability.

In Fig. 6, you will observe that from time to time both auricular and ventricular contractions are lacking. The explanation of this failure to contract is held to be depression of the excitability. The normal stimulus production is maintained as shown by the regular sinus rhythm. Extra systoles of all kinds are obviously absent. The force of the various contractions is unaltered, hence there can be no impaired contractility, nor is conductivity affected, since at every contraction it is seen that the various cardiac chambers follow each other in quick succession. By exclusion, therefore, the only remaining possibility for such an irregularity is deficiency of excitability. Englemann compared excitability to the primer in the old time flint lock muskets, the stimulus he likened to the hammer and the latent energy or stored up contractility of the heart muscle he called the charge of powder. Continuing his analogy to this arrhythmia he says, "the amount of primer in the gun is too small, so that the hammer when it strikes produces no explosion."

A typical and readily recognized form of irregularity may result

when the fourth fundamental property for heart muscle, contractility, is impaired. A strong pulse beat is followed by a weaker one, giving a characteristic radial tracing (Fig. 7). Further, the interval between the small beat and the next large beat is noticeably longer than is the interval between the large and small beats. The explanation for this lies in the fact that, if through weakness of the cardiac muscle the power to contract is impaired, whenever a forcible contraction takes place such a contraction continues so long that it lessens the length of the period of rest that should occur, as a result the next stimulus finds the contractility insufficiently restored, hence the muscle cells are only able to execute a short weak contraction. This short contraction, however, gives the heart a chance for a longer rest, so that when the next stimulus arrives a forcible impulse of long duration may again occur. To this form of irregularity, in which a small beat follows a longer one, has been applied the name of *pulsus alternans*. It is an extremely rare form

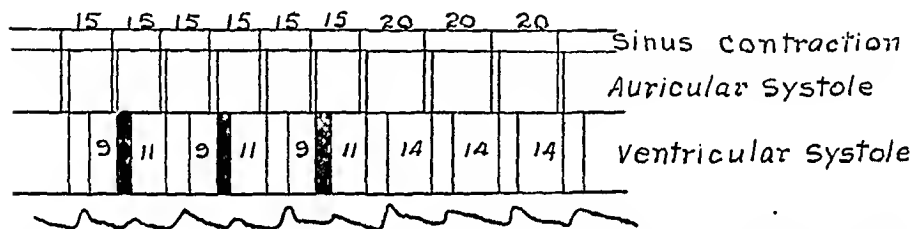


FIG. 7.—Impaired contractility giving rise to the *pulsus alternans*. The small contractions are shaded. Note that the condition occurs only at the time when the normal sinus rhythm is quickened, the cardiac cycle requiring only 15 time units instead of 20.

of irregularity, only found when the rate of the heart is rapid, frequently disappearing when the rate slows down, and indicating a grave degree of cardiac exhaustion. Many reported instances of *pulsus alternans* are in reality the results of recurring extra systoles.

Impairment of the property of tonicity does not give rise to any characteristic irregularity. Failure of this function results in a greater or less degree of cardiac dilatation with its obvious physical signs and symptoms.

We have then taken up a group of cardiac irregularities which have been shown beyond reasonable doubt to definitely result from perversion or failure of the five cardinal functions of cardiac muscle as understood in the myogenic doctrine.

There remains, however, one more form of arrhythmia to which attention should be called because of its great frequency and clinical importance. I refer to the cases of so-called complete permanent irregularity or *arrhythmia perpetua*. In these the fundamental rhythm is completely destroyed. The condition is found in severe heart failure such as supervenes in the later stages of chronic endocarditis of rheumatic origin. The irregularity of the pulse is hopelessly confusing and follows no apparent order (see Fig. 8). In

the venous pulse it is noteworthy that there is an absence of the wave due to auricular contraction, from which it has been inferred that the auricles are either paralyzed or become so engorged that their action is embarrassed (Fig. 8 *a*). The most tenable explanation for this remarkable irregularity was until recently the one offered by Mackenzie. He asserted that there is ample evidence that in these cases the starting point for the cardiac rhythm is no longer at the remains of the sinus venosus, but is transferred lower down to the auriculo-ventricular node. This abnormal inception of the cardiac rhythm causes auricles and ventricles to contract almost

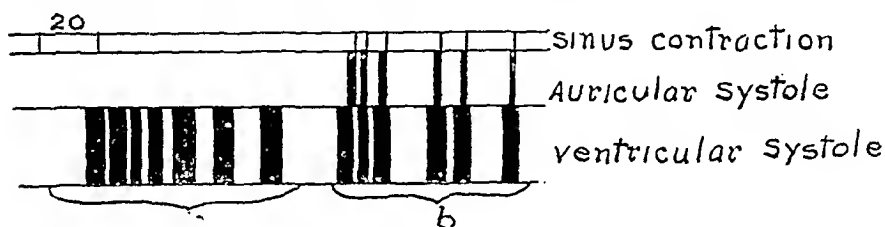


FIG. 8. Arrhythmia perpetua or complete irregularity. Note the complete destruction of the normal fundamental sinus rhythm, and the auricular paralysis illustrated at *a*, whereas the theory that this irregularity is due to an abnormal inception of the cardiac rhythm at the auriculo-ventricular node is shown at *b*.

simultaneously, the ventricular systole preceding that of the auricle by about 0.1 seconds (Fig. 8 *b*). To this continuous irregularity of the heart he applies the term nodal rhythm. More recently he has subscribed to the view of Cushny that such irregularity is the result of auricular fibrillation, a condition now demonstrable by the electrocardiogram.

Numerous other forms of arrhythmia have been described, as for example hemisystoles, disassociation between the right and left sides of the heart, the various tachycardias, as paroxysmal tachycardia, and the bradycardias. Some of which, no doubt, are due to the fibrillation above mentioned. But, in our present state of uncertainty regarding their cause, any attempt to discuss them would result only in confusion.

THE INTERRELATION OF THE ORGANS OF INTERNAL SECRETION.

I. THE THYROIDS

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SINCE the middle of the nineteenth century, a vast array of observations, clinical and experimental, has been collected in the endeavor

to elucidate the functions of the organs of internal secretion. The problems have been difficult and progress toward their solution has been correspondingly slow. From a long series of observations, however, on the effects of extirpating various individual organs, and of artificially supplying an excess of their substance to experimental animals, a fairly adequate knowledge of the general functions of most of the glands has been secured. This information has been largely supplemented by clinical observations on the effects of excessive or depressed functioning of the organs.

The correlated problems, however, the means whereby the activities of the various glands are controlled, have progressed toward solution by no means so satisfactorily. Despite the great extent of the present day literature on internal secretion it is impossible to say of any one of the individual organs just how this control is mediated. That different glands react to chemical conditions in the body is known in certain cases; the thyroid hypertrophy that occurs during pregnancy is an instance. Signs of increased activity have been noted also in the hypophysis after the administration of certain toxins. But the organs also respond to nervous influences. For instance, an increased amount of the characteristic secretion of the adrenals has been noted in the blood after stimulation of the splanchnic nerve. From the fact, however, that various ductless glands can function effectively as grafts when there is no possibility of nervous control, it appears that such control is of subsidiary importance.

In certain organs of external secretion, chemical control is known definitely to occur, and in the present state of our knowledge, the theory that the organs of internal secretion are largely subject to hormone control is attractive, and seems not improbable. In regard to the possible sources of such hormones, very little is known. It has often been suggested that different ductless glands have a function of neutralizing endogenous toxins. If this were true, these toxins would in a measure come within the definition of hormones.

There is considerable evidence that the secretions of certain of the organs of internal secretion themselves serve as hormones for other organs. The evidence consists partly of the results of animal experimentation, and partly of clinical observations. It is scattered through a wide range of publications, clinical, pathological, and physiological. This paper embodies an attempt to assemble and evaluate this evidence. The endeavor has been to consider somewhat exhaustively the literature dealing with the subject from the experimental side, and the clinical literature has been utilized for such observations as bear directly upon the various points discussed. An attempt has been made to eliminate that speculative element, which always flourishes in the earlier stages of a literature.

THE THYROID.

The evidence of interrelationships involving the thyroid is more extensive and better established than in the case of any of the other endosecretory organs (that is, organs of internal secretion). The thyroid will be discussed in relation to the adrenals, the hypophysis, the gonads, the thymus, and the pancreas.

THYROID—ADRENALS. The relationship between the thyroids and adrenals has been studied somewhat extensively of late, particularly by German investigators. Both experimental and clinical data have been utilized.

Laignel-Lavastine¹ has recently cited a number of cases in which clinical symptoms or autopsy findings indicate an association of pathological conditions in both glands, but such cases are too infrequent to have much value as evidence; many instances of association of morbid conditions in two organs are required to establish any presumption of a specific relationship between them.

Hypothyroidism. The first experimental investigation of the effect of hypothyroidism upon the adrenals was made apparently by Hofmeister² in 1894. A large number of thyroidectomies were made upon young rabbits and the results studied in various organs. No effect at all upon the adrenals was established. This finding was specifically confirmed by Bensen³ who made a similar study in 1902. Many other cases of experimental thyroidectomy have been reported, and since no morphological effects in the adrenals have been noted, presumably none occur.

The matter has been studied in another way by Bruckner⁴ who performed thyroidectomies upon ten dogs, and then investigated their blood to determine the adrenalin content. He used the Meltzer-Ehrmann test, with the frog's eye, and the chemical test of Schur and Wiesel. His findings by both these methods were negative, and he concluded that thyroidectomy had depressed the adrenal functioning. He apparently used no controls, however, and his conclusions are in themselves of doubtful validity.

Hyperthyroidism. Rudinger, Falta, and Eppinger⁵ have recently proposed a theory that the thyroids, pancreas, and adrenals are intimately related. As a result of a large number of experiments involving thyroid and pancreas extirpations and the administration of adrenalin and thyroid substance they have concluded that the pancreas inhibits both the thyroids and the chromaffin system—of which the adrenals are the chief members; the adrenals inhibit the pancreas and stimulate the thyroids while the thyroids also inhibit the pancreas and stimulate the adrenals.

¹ Gaz. d. hôp. d. Paris, 1908, lxxxix, 1563.

² Virchow's Arch., 1902, clxx, 229.

³ Zeit. f. klin. Med., 1908, lxxiv, 1.

⁴ Beitr. z. klin. Chir., 1894, xi, 463.

⁵ Comp. rend. Soc. Biol., 1908, lxxiv, 1123.

The theory in regard to the thyroid-adrenal relationship is supported by the recent work of several other investigators. Kraus and Friedenthal⁶ have found that normal human blood serum has no effect upon the frog's eye, but after the injection of thyroid extract there is developed in the blood a marked mydriatic power, supposedly due to an increase in the adrenalin content. Caro⁷ has confirmed this observation in dogs and rabbits, using both the frog's eye and iron-chlorid tests. Frankel⁸ has made a series of graphic studies of the effects of adrenalin on rabbit's uterus. By this method he was able to demonstrate in three cases of Basedow's disease, an increase in the adrenalin content of the blood of 400 to 800 per cent.

Selzer and Wilenko,⁹ however, using the Meltzer-Ehrmann test were able to demonstrate epinephrinemia in only 1 of 4 typical cases of Basedow's disease.

Kostlivy¹⁰ in 42 cases of thyroid intoxication, found in general an increase in the mydriatic power of the blood serum. In several of these cases thyroidectomy was performed. The operation resulted in a marked decrease in the pupilodilator substance. In rabbits treated *per os* with thyroid substance he noted an increase in the mydriatic power of the serum proportional to the dosage. In six dogs he found in the serum after intravenous injection of thyroid material from 4 cases of Basedow's disease a similar increased mydriatic substance. At autopsy the adrenals of his rabbits showed marked hypertrophy. Delille,¹¹ however, in rabbits has found thyroid extract to have little effect on the adrenals.

An effect similar to that obtained by Kostlivy in rabbits has been noted by the writer in a series of 18 experiments upon young guinea-pigs. He has found also¹² in the offspring of female guinea-pigs that had been fed with varying amounts of thyroid substance a depression in the weights of the adrenals, roughly corresponding with the dosage. This effect has been interpreted as a reaction to epinephrinemia caused by the thyroid medication in the mother.

In opposition to the foregoing observations, Hoffman¹³ has noted also in myxedema and in thyroidectomized animals an increase in the mydriatic power of the blood. A possible explanation of the apparent conflict, however, lies in the fact noted by Biedl, Zandler, and Ranze¹⁴ that both pituitary and thymus extracts give the Meltzer-Ehrmann reaction, and, as will be discussed later, there is reason to think that hypothyroidism results

⁶ Berl. klin. Wochens., 1908, xlv, 1710.

⁷ Med. klin. Berl., 1910, vi, 136.

⁸ Arch. f. exp. Pathol. u. Pharmacol., 1909, ix, 395.

⁹ Wien. klin. Wochens., 1910, xxiii, 586.

¹⁰ Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1910, xxi, No. 4.

¹¹ La hypophyse et médication hypophysaire, Paris, 1909.

¹² Hoskins. Amer. Jour. Physiol., 1910, xxvi, 426.

¹³ Zeit. f. klin. Med., 1910, lxxix, 359.

¹⁴ Cited by Kostlivy.⁽¹⁰⁾

in an increased activity of the pituitary, and possibly, thereby an increased production of the pupilodilator substance.

On the whole, the existing evidence although not entirely concordant indicates fairly convincingly that the thyroid through its internal secretion stimulates the adrenals.

THYROID—PITUITARY. The existence of a relationship between the thyroid and the hypophysis is perhaps the most satisfactorily demonstrated of all the possible interrelations of endosecretory organs. The experimental evidence is somewhat extensive, and is fairly well supported by clinical observations.

Hypothyroidism. Twenty years ago when Rogowitsch¹⁵ found that after thyroidectomy the pituitary hypertrophied, he suggested in explanation that this organ was functioning vicariously for the thyroid. A full discussion of all the clinical observations bearing upon the point is not possible, but a few cases may be referred to. The results reported by Boyce and Beadles¹⁶ in 1893 have often been cited. They found that in 2 cases of myxœdema and 1 of sporadic cretinism, the thyroids were atrophic, while the pituitaries showed marked hypertrophy. Both Schönemann¹⁷ and Comte¹⁸ studied large series of thyroids and pituitaries from cases of various sorts showing thyroid atrophy. Schönemann noted that in 112 cases a considerable number showed hypertrophy of the pituitaries, the effect being confined to the anterior lobe of the organ. Comte found in 108 cases that the pituitary was generally hypertrophied when the thyroid showed atrophy. He interpreted this hypertrophy as supporting Rogowitsch's theory of vicarious functioning of the pituitary. Bourneville and Brisson¹⁹ described in detail the conditions in a case of myxœdema, which support the same conclusion; there was thyroid atrophy with a marked hypertrophy of the pituitary. Similar conditions have been reported by Pisenti and Viola²⁰ in a case of *stroma fibrosa*, and by Calderara²¹ in a case of myxœdema. The pituitary contained an abnormal amount of colloid in both cases, and in the case of myxœdema the organ also showed evidence of secretory activity in the notable abundance of the chromophile cells of the epithelial lobe. Gourfein-Welt²² reports a case—and cites several others—in which myxœdema with, of course, thyroid deficiency, was accompanied by ocular symptoms, indicating that the pituitary was hypertrophied and was causing pressure on the optic chiasma.

Although the clinical findings of pituitary hypertrophy with thyroid deficiency are frequent, the relation cannot in all instances be demonstrated. In the cases of five cretins studied by de Coulon,²³

¹⁵ Beitr. z. path. Anat., 1889, iv, 453.

¹⁶ Jour. Path. and Bact., 1893, i, 223.

¹⁷ Virch. Arch., 1892, cxxix, 310.

¹⁸ Beitr. z. path. Anat., 1898, xxiii, 90.

¹⁹ Arch. d. Neurol., xii. Cited by Gourfein-Welt. (??)

²⁰ Centralbl. f. d. med. Wiss., 1890, pp. 450, and 481.

²¹ Arch. Ital. d. Biol., 1908, I, 190.

²² Arch. d'ophtalm., Paris, 1907, xxvii, 561.

²³ Virch. Arch., 1897, cxlvii, 53.

the pituitaries were normal, or possibly slightly below average size. Ponfick²⁴ has reported a careful study of a case of myxoedema, in which he found—in connection with a typical atrophy of the thyroid—a *degeneration* of the hypophysis. It is evident, therefore, that from the clinical literature alone, no final conclusions can be drawn. A great many cases are reported in which both thyroid and pituitary show coincident structural alterations, but to what extent these conditions stand in causal relationship to each other, and to what extent they are due to a common cause, cannot be determined.

Experimental data in regard to the effects of thyroid deficiency are available in considerable quantity. The results obtained by Rogowitsch have been referred to. His findings of pituitary hypertrophy following thyroidectomy has often been confirmed, but there is much disagreement as to which constituents of the hypophysis are affected. Rogowitsch described the enlargement of the pituitary as due to hyperplasia of certain "Kernhaufen" (masses of small "chromophobe" cells) of the anterior lobe. He found also an increased amount of colloid formed by the chromophile cells of this lobe, and a general vacuolization of the parenchyma. Stieda²⁵ repeated the experiment upon seven rabbits. He described the hypertrophy, which he also obtained, as due to an increase in the number of "Hauptzellen" or "chromophobe" cells of the anterior lobe, with a vacuolization of their protoplasm; he states that the chromophile cells were not affected, and that there was no colloid formation. Tizzoni and Centanni²⁶ performed similar experiments upon two dogs and noted at autopsy, one and one-half and four years, respectively, after the operations, results similar to those of Rogowitsch except that there was a marked diminution of "chromophobe" cells. Gley,²⁷ Leonhardt,²⁸ and Hofmeister, have obtained similar hypertrophy with rabbits; Hofmeister noted an augmentation both in number and volume of the cells. These findings have since been confirmed by Alquier²⁹ in the dog, and by Thaon³⁰ in the ram. Similar results have been reported by Horsley, v. Eiselsberg, and Lusena.²⁹ Cimatori³¹ noted the same effect in the dog and the rabbit. In a careful study of the histological changes resulting from thyroidectomy he found in the anterior lobe many voluminous "chromophobe" cells, among which were intercalated here and there, others of the eosinophile and cyanophile types. These elements were more or less vacuolated, giving appearances which this observer regarded as evidence of enhanced secretory activity. Torri³² noted after

²⁴ Zeit. f. klin. Med., 1899, xxxviii, 1.

²⁵ Cited by Delille.

²⁶ Virch. Arch., 1897, cxlix, 341.

²⁷ Cited by Delille.

²⁸ Cited by Delille.

²⁹ Beitr. f. path. Anat., 1890, vii, 537.

²⁷ Arch. d. physiol., 1892, xxiv, 664.

²⁹ Jour. physiol. e. pathol. gén., 1907, ix, 492.

³¹ Arch. Ital. d. Biol., 1907, xlviii, 387.

the same operation in the dog and the cat, a hypertrophy marked by increase in the number of chromophile cells and an augmented secretion of colloid. Herring³³ has recently published results that are notably different from those previously mentioned. He has found that after thyroidectomy the *anterior lobe* of the pituitary is quite unaffected. There is, however, an increased activity—and probably a numerical hypertrophy—of the cells of the *pars intermedia*. In the so-called “nervous” part of the posterior lobe, and in the floor of the third ventricle, appear numerous granular, hyaline, or colloid bodies that seem to arise from the epithelial cells of the *pars intermedia*. The ependyma and neuroglia cells of this lobe proliferate and the former secrete globular bodies into the cavity of the lobe. Despite the variations in details, the clinical and the experimental data appear to indicate rather conclusively that the pituitary hypertrophies as a reaction to hypothyroidism. As to what part of the pituitary is affected further evidence is needed.

Hyperthyroidism. Very little evidence has been found in regard to the effects of hyperthyroidism on the hypophysis. Guerrini³⁴ after injections of thyroid extract in various animals noted a hypertrophy of the pituitary—but since he got a similar effect by injecting pilocarpine and other poisons, he regards it as merely a reaction to the thyroid as a toxin. Delille states that in rabbits treated with thyroid, the hypophysis shows at first a slight hyperplasia, but soon reaches a state of exhaustion. This evidence, so far as it goes, indicates that hyperthyroidism stimulates the pituitary to increased activity, but it is too slight in quantity to be at all significant.

There is, on the whole, little doubt of the existence of some sort of specific relationship between the two glands. If we accept Guerrini's explanation of the effect of hyperthyroidism upon the hypophysis, the recorded observations support very well the theory of Rogowitsch that the pituitary in case of need functions vicariously for the thyroid. This evidence, however, does not exclude a theory that the thyroid exercises normally an inhibition upon the pituitary and that the hypertrophy noted in hypothyroidism is due simply to the removal of this check upon its activity. In either case, the hypertrophy would be primarily a reaction to increased functioning. From the fact that symptoms of hyperpituitism are not present as a result of hypothyroidism it appears that the organ as a whole, does not participate in the increased activity.

THYROID—GONADS. It has long been thought by clinicians that some sort of relationship exists between the thyroid and the sex glands. In cases of Basedow's disease, when the thyroid activities

³³ Quart. Jour. Exp. Physiol., 1908, i, 284.

³⁴ Arch. ital. d. biol., 1905, xliii, 1.

are abnormal, the sex functions likewise are often affected. Many clinical observers mention menstrual disturbances during the course of this disease. The literature on the subject has recently been discussed at length by Sattler,³⁵ who thus summarizes his observations: Menstrual conditions in Basedow's disease: Trousseau: All cases show anomalies. Griffith: In 28 cases, 6 showed amenorrhœa. West: In 38 cases, many showed irregularities. Russell: In 48 cases, the majority were regular in this function. Murray: In 170 cases, 45 showed irregularities and 24, amenorrhœa. Mannheim: In 36 cases, 19 were normal. Koehler: Many show irregularities (according to Kron,³⁶ 3 only in 72 of Koehler's cases were normal in this respect). Möbius thinks that menstrual disturbances are no more frequent in Basedow's disease than in any other equally serious illness. Oppenheim regards amenorrhœa as unusual in this disease.

Rogers³⁷ has recently reported that, in his experience, menstrual disturbances with enlarged and tender ovaries always occur in Basedow's disease.

While these observations are by no means unequivocal they support to some degree the idea that menstrual disturbances are characteristic of Basedow's disease. Rather more significant is the fact that actual atrophy of the sex organs often occurs in this malady. A great many instances of this are on record, but an enumeration of them would hardly be within the province of the present work. (For full discussion, with summary, cf. Sattler, p. 275.)

In myxœdema, of which hypothyroidism is the cause, sex depression may be so pronounced as to amount to complete impotence. Gandy³⁸ has recently described 2 cases that illustrate this fact convincingly. His two patients, men, aged twenty-five, and thirty-three years, respectively, after having attained normal adult sexual condition, developed myxœdema, which was followed by a complete reversion to sexual infantilism marked by atrophy of the genitalia and, of course, impotence. Many other cases of an association of infantilism with thyroid deficiency are on record. The fact, noted by Caro³⁹ and others, that in such cases the sex depression can be ameliorated by thyroid medication, indicates rather conclusively that hypothyroidism is the actual cause of the condition. The clinical evidence on the whole, supports the idea that the gonads are affected by the thyroid. If, however, Basedow's disease represents, as is usually supposed, a condition of hyperthyroidism, the evidence is equivocal.

³⁵ Basedowsche Krankheit., Leipzig, 1909, vol. i.

³⁶ Berl. klin. Wochenschr., 1907, xlv, 1611, 1651.

³⁷ Jour. Amer. Med. Assn., 1910, liv, 1893.

³⁸ Berl. klin. Wochenschr., 1905, xlii, 310.

³⁹ Gaz. d. hôp. d. Paris., 1906, p. 1687.

Various attempts have been made—notably by French investigators—to determine the relationship between the ovaries and the thyroids by a comparison of their influences upon metabolisms. As yet, however, this method has thrown no satisfactory light upon the question. Parhon and Goldstein⁴⁰ have concluded from a study of the literature and from various observations of their own that there exists a distinct antagonism between the glands. Charrin and Jardry⁴¹ however, among others, have reached the opposed conclusion that the organs are synergetic. Further study of the question is needed.

Experimentally, thyroidectomy has given, in the hands of various observers, a depression of the sex function with atrophy or degeneration of the gonads. Such findings have been reported by Hofmeister in the case of young rabbits, and by Lanz⁴² in goats. Lanz reports also the case of a man who had reached a cretinoid state ten years after thyroidectomy, in whom the testes were markedly atrophic. Ceni⁴³ has noted a decided lessening of the production of eggs after thyroidectomy in hens. Alquier and Theureny⁴⁴ have reported that in *adult* or *aged* dogs, they have been unable to demonstrate any effect upon the ovaries after thyroidectomy. They had previously reported,⁴⁵ however, that a marked depression of activity in the testes occurs under such conditions.

On the whole, it seems evident from clinical and experimental data, that there exists some sort of a relationship between these two organs, and it is probable that the thyroids have on the sex organs a stimulating effect that is necessary for the normal continuance of their functions.

THYROID—THYMUS. The evidence of a relationship between the thyroid and thymus is, as in other cases discussed, partly clinical and partly experimental. In cases of Basedow's disease, the thymus is often hypertrophied. Apparently this was first noted by Cooper⁴⁶ in 1832. Many similar instances of this association of abnormal conditions in the two glands have since been reported. In their broad features, all the reports consulted by the writer are essentially the same. They describe ordinary cases of Basedow's disease, with thymus hypertrophy in addition, and often with the lymphoid organs in general similarly affected. Such findings have been recorded, among others, by Markham,⁴⁷ Walz-

⁴⁰ Arch. gen. med. ann., 1905, lxxxii, 142.

⁴¹ Comp. rend. acad. sc., Paris, 1906, cxlii, 1442.

⁴² Arch. f. klin. Chir., 1904, lxxiv, 886.

⁴³ Arch. Ital. d. Biol., 1905, xlii, 420.

⁴⁴ Comp. rend. Soc. d. biol., 1909, lxvi, 217.

⁴⁵ Ibid., 1908, lxiv, 663.

⁴⁶ The Anatomy of the Thymus Gland, London, 1872. Cited by Hart; Münch. med. Wochens., 1908, iv, 668

⁴⁷ Trans. Path. Soc., London, 1858, ix.

berg,⁴⁸ Mosler,⁴⁹ Mobius,⁵⁰ Gueneau de Mussy,⁵¹ Hirschlaff,⁵² Pansini and Benenati,⁵³ Hansemann,⁵⁴ and Gierke.⁵⁵ Capelle⁵⁶ has recently attempted to analyze the literature of Basedow's disease in regard to the frequency with which thymus hypertrophy occurs. He was able to collect 60 cases with available autopsy records. Of cases in which the patients had died of an intercurrent affection, 44 per cent. showed thymus hypertrophy; of those dying directly of the disease, 82 per cent., and of those that succumbed to surgical interference, 95 per cent. showed this condition. Pappenheimer⁵⁷ has recently made a histological study of the thymuses of three patients who had Basedow's disease associated with *status lymphaticus*. The organs showed "renewal of growth" rather than mere persistence.

Not only in acute hyperthyroidism does thymus hypertrophy occur; it may also be associated with simple congenital goitre. In Switzerland, where this disease is endemic, the offspring of goitrous mothers often have both thymus and thyroids enlarged.⁵⁸ Marine and Lenhart⁵⁹ report a similar condition in young animals in which spontaneous thyroid hyperplasia is found. Whether, however, the simultaneous hypertrophies in the two organs are equally reactions to a common cause, or whether the hyperactivity of one is a cause of the similar state in the other cannot from such observations be determined.

So far as the writer has been able to ascertain, no direct attempt has been made to determine experimentally whether hyperthyroidism would cause thymus hypertrophy. In a series of experiments previously referred to, the writer found that the offspring of female guinea-pigs treated with thyroid substance have hypertrophied thymuses. This fact seems to indicate that the thyroid stimulates the thymus. The converse method of testing the relationship, that is, by hypothyroidism, has been reported only a few times and the resulting evidence is conflicting. If thyroid activity excites thymic activity, thyroidectomy, by removing a normal stimulus would be expected to cause thymic atrophy. Gley,⁶⁰ in 1894, reported a few experiments upon dogs and rabbits, and Cadéac and Guinard,⁶¹ in the same year, made similar investigations upon

⁴⁸ Klin. Monatsbl. f. Augenheilk., 1876, iv, 401.

⁴⁹ Schmidt's Jahrb., 1889, 223, 521. Cited by Möbius.⁵⁰

⁵⁰ Spec. Path. u. Therapie (Nothnagle), xxii, 44.

⁵¹ Bull. et mem. Soc. thérapeutique, 1881, xiii, 218.

⁵² Zeit. f. klin. Med., 1899, xxxiv, 200.

⁵⁴ Berl. klin. Wochens., 1905, xlv, 65.

⁵⁵ Münch. med. Wochens., 1907, liv, 775.

⁵⁷ Jour. Med. Research, 1910, xxii, 1.

⁵³ Policlin (M.), 1902, ix, 216.

⁵⁶ Ibid., 1908, lv, 1826.

⁵⁸ Birnbaum. Klinik der Missbildungen und kongenitalen Erkrankungen den Fötus, Berlin, 1909, p. 91.

⁵⁹ Arch. Int. Med., 1909, iv, 253.

⁶⁰ Comp.-rend. soc. de biol., 1894, xlix, 528.

⁶¹ Ibid., 508.

two lambs, from which they concluded that hypertrophy of the thymus follows thyroidectomy; but their data are inadequate. Hofmeister on the other hand, after a much more extensive series of experiments upon young rabbits, obtained no such result. In direct contradiction to the observations of the first mentioned investigators, Jeandelize, Lucien, and Parisot⁶² have recently noted that thyroidectomy in seven young rabbits caused in every instance a diminution of the weight of the thymus, as compared with that of a control animal of equal size. Worms and Pigache⁶³ also have reported a few experiments of similar import. In their animals the thymuses a few days after thyroidectomy were found degenerated; the parenchyma was largely replaced by connective tissue. On the whole, the experimental observations add little to the clinical evidence, and it remains for the present an open question whether thyroid conditions have any direct effect upon the thymus.

THYROID—PANCREAS. The fact that thyroid conditions affect carbohydrate metabolism has been interpreted by a number of observers recently as indicating a relationship between the thyroid and the pancreas. Sattler (p. 294) cites many instances in which thyroid medication has caused glycosuria. Eppinger, Falta and Rudinger, Grey and de Sautelle⁶⁴ have noted that the glycosuria ordinarily produced in dogs by large doses of adrenalin no longer occurs after thyroidectomy, providing incidentally, that the parathyroids are left intact. Underhill and Hilditch,⁶⁵ however, have entirely failed to confirm this work. Pick and Pineles⁶⁶ have been able to confirm it in goats, but not in rabbits. Of similar significance for the present theme, is the observation of McCurdy⁶⁷ that thyroidectomy raises the assimilation limit for dextrose. Siegmund⁶⁸ has recently described the cases of two children in whom a pronounced "sugar hunger" was caused by thyroid deficiency, and in whom the condition was promptly relieved by thyreoidin. The evidence on the whole, is favorable to the theory that the thyroid inhibits the pancreas, in its function of promoting glycolysis. Whether there is a selective involvement of the islands of Langerhans is questionable. Falta⁶⁹ has reported one case in which after thyroidectomy an undoubted hypertrophy of the islands was found, but more data are required for any final conclusion.

In summary it may be said that most of the available evidence indicates that the thyroid stimulates the adrenals. Hypothyroidism causes hypertrophy in the pituitary, probably due to a vicarious assumption of thyroid function. It is fairly well demonstrated that

⁶² *Comp.-rend. soc. de biol.*, 1909, lxvi, 942.

⁶⁴ *Jour. Exp. Med.*, 1909, xi, 798.

⁶⁶ *Biochem. Zeit.*, 1908, xii, 473.

⁶⁸ *Deut. med. Wochensh.*, 1910, xxxvi, 990.

⁶⁹ *Wien. klin. Wochensh.*, 1909, xxii, 1059.

⁶³ *Ibid.*, lxvii, 500.

⁶⁵ *Amer. Jour. Physiol.*, 1909, xxv, 66.

⁶⁷ *Jour. Exp. Med.*, 1909, xi, 798.

there is a relation between the thyroid and the gonads, which are probably stimulated to normal activity by the former. The frequent association of abnormal conditions in the thyroid and thymus points toward a relationship between them, but definite evidence upon the point is meagre and conflicting. The theory that the thyroid inhibits the pancreas is probable, but more data are needed.

FURTHER OBSERVATIONS ON ACETABULAR FRACTURE WITH INTRAPELVIC OR CENTRAL DISLOCATION OF THE FEMORAL HEAD.

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Most fractures of the pelvic ring with or without injury to the structures in the pelvic cavity are relatively common. The symptoms and signs characteristic of this injury are fairly constant and usually sufficient to satisfactorily settle the question of diagnosis. On the other hand, isolated fractures of the floor of the acetabulum permitting the entrance of the femoral head into the pelvic cavity are rare, exceedingly difficult to diagnose, and, like pelvic fractures, frequently entail danger to life.

The infrequency of acetabular fracture has not permitted exhaustive or extended study of this injury. A few surgeons have seen at most but 2 or 3 cases; many surgeons have not seen a single case. It follows, therefore, that a typical clinical picture of this injury, if such there be, is far from a clear one, and possibly is yet unknown.

Schroeder¹ has collected about 50 cases, including 3 of his own, which have been reported under this title. It will be found that this collection contains many cases reported before we had the aid of the *x*-rays; that others are included in which observations were made on clinical grounds alone, without operation or autopsy to confirm the diagnosis. Moreover, this collection contains cases which, strictly speaking, belong in no sense to acetabular fractures. Many of them were pelvic ring fractures of various kinds and descriptions, which, of course, caused central dislocation of the femoral head, but only by virtue of large sections of the pelvic bones giving way under the violence and not merely by fractures of the acetabulum.

Fractures of the pelvic bones, as ordinarily met with, have a mechanism in their production not the same as that of acetabular

¹ Northwestern University Medical School Bulletin, June, 1909.

fractures. The symptoms of the former injury are more pronounced, and the complications to the pelvic contents usually more severe. Again, the treatment, when conducted in accordance with the indications in the two injuries is, or should be, along lines entirely different.

The one indispensable prerequisite to intelligent and successful treatment in traumatic bone lesions near the wrist-joint is specific knowledge concerning all details of such a lesion. Clinical evidence of injury here must be unerringly recognized, and confirmed by skiagrams, operation, or both, if the best results in the treatment are to be had. This is no less true of the elbow-joint, the shoulder, and, above all, the hip-joint.

May not the high rate of mortality heretofore ascribed to acetabular fracture be due, in part at least, to lack of discrimination in studying injuries of the pelvis and hip? It is perfectly plain that acetabular fracture or pelvic ring fracture, without complications, should be attended by a very low, or possibly no mortality. Death in such injuries is due as a rule, to injuries implicating the pelvic contents—the urethra, the urinary bladder, intestines, and blood-vessels.

The fracture, therefore, discussed in this paper, is not such as involves the pelvic bones as generally seen after severely crushing injuries, but fractures of the acetabulum due to indirect violence acting through the femur, and through which fracture the femoral head is driven into the pelvic cavity. Not to thus distinguish this lesion is about equivalent to viewing, for instance, all fractures at the lower end of the radius as Colles fractures; and fractures at the shoulder, whether of the shaft of the humerus, its anatomical or surgical neck, or fractures of the scapula, as one and the same fracture. Fulfilment of the indications for treatment presented by a fracture, as we view this lesion at the present time, is not accomplished by the haphazard methods in vogue two or more decades ago. Then fractures were "treated" often without definite knowledge of their kind, character, and sometimes without knowing their exact location. Complications, if not entirely overlooked, were often as unskilfully managed as the fracture itself.

It was then, let us hope, that those elaborate devices known by the name of manufactured splints, ornamented with gaudy leather straps supporting showy buckles, had their day. Too often, indeed, these gilded trappings covered fractures unreduced, and limbs possibly not fractured at all; in hiding from view the ugliness and deformity that only mismanaged fractures exhibit, the very pretentious and showy appearance of many of these useless things too often begot that false sense of security and self-satisfied feeling, seen sometimes even now, in the easy-going medical man.

Satisfactory treatment of a fracture today presupposes a knowledge of the force or violence which produces the fracture, its exact

location, type, and kind, as well as its complications. Moreover, it presupposes familiarity with those mechanical means which, when applied, with or without operative interference, will securely and permanently hold all broken fragments of bone in proper relation to one another. No other plan of procedure in bone work has succeeded, and probably no other can succeed.

Differential diagnosis *must* be made before we successfully terminate abdominal affections. Appendectomy does not abate the symptoms nor relieve the distress of ureteral stone, although not apparent to some till the experiment is tried. Colostomy does not relieve an ileus if placed on the distal side of the obstruction; yet, strange as it may seem, this, too, has been tried. Nor is this all. The indiscriminate grouping of all pelvic fractures will add little to our knowledge of acetabular fracture. Much of our knowledge of traumatic bone lesions in general is concise and practically complete; but few unimportant details are yet wanting. Nor was this subject clarified by regarding all fractures of a given bone as one lesion, but only by differentiating them; by studying them singly and individually as to their manner of production, their diversified and dissimilar clinical manifestations, which usually provide adequate therapeutic measures, and which necessarily follow systematic inquiry into most all surgical conditions.

In order to assign the fracture under discussion to this category it must be viewed as an isolated fracture possessing peculiar characteristics of its own. Acetabular fracture is produced by force acting through the femur or its trochanter. It is true that it may exist or be found as an additional injury to other pelvic fractures which follow severe crushing injuries, but, as such, is merely a complication or is one of a multiple fracture and is devoid of the interest attaching to isolated fractures of the acetabulum. Two interesting cases of this class are the following:

CASE I.—On February 2, 1909, I saw in consultation with Dr. John E. Haskell, of Chicago, a man who, the day previous, had received a severe injury by a fall from a height of about thirty feet. This man was twenty-nine years old, strong, muscular, and weighed 160 pounds. While at work on the day mentioned he fell from the top of a telephone pole, striking the ground squarely on the bottom of the right foot, with the right leg slightly abducted and the body inclined toward the right. Consciousness was not lost; he was able to rise from the ground, but suffered intense pain in the region of the right hip-joint. Twenty-four hours later I saw him, and found his condition to be as follows:

General appearance good; pulse, 80; temperature, 99°. He was perfectly rational, but complained of headache. There was nausea and vomiting; the vomited matter contained some blood, which had its origin in a slight injury of the nose, and which at the time of bleeding had been swallowed. The upper half of the body,

including the extremities, presented evidence of no further injury. The right lower portion of the abdomen was tense, tender, and dull on percussion. The right leg was the shorter by 2 or 3 cm., and was slightly everted, although the patient could partially invert the foot at will. Measurements of both legs showed the difference in length to be slight. The patient was not able to abduct, adduct, flex, or extend the injured leg, although these movements could be executed by seizing the limb and placing it in any of the desired positions.

A prolonged but successful attempt to catheterize the patient demonstrated a ruptured urethra very close to the bladder. Several ounces of urine were drawn off, and repeated filling of the bladder with boric solution demonstrated that the bladder itself was unruptured. The catheter was left in the bladder for one week, during which time frequent bladder irrigations were carried out. There were no contusions of the soft parts about the buttocks, hips, or perineum; the skin over these regions was not abraded.

A few symptoms, not particularly characteristic of dislocation of the hip, nor of fracture of the neck of the femur, were present. One very important sign was noted, and that was the sunken appearance of the trochanter, a feature *in central dislocation of the femoral head* emphasized by several writers. This, I think, is a sign of great importance, and when considered with other points later to be mentioned, should go far toward establishing the diagnosis. The only lesion below the pelvis was found on the right heel, which was swollen, tender to touch, and showed considerable hemorrhage under the skin below the ankle.

The nature of the hip injury was not clear, and for a better understanding of the condition the patient was anesthetized. All of the measurements were then repeated, with same findings as before. Rectal examination was again carefully made, but disclosed nothing abnormal; the injury was thought to be a deeply impacted fracture of the neck of the femur or a dislocation of the femoral head into the pelvic cavity. The latter possibility was suspected because of the nature or manner of the accident, the comparative freedom of motion of the limb in all directions, and the ruptured urethra; but more particularly owing to an observation made in hyperextending the thigh. This position, obtained by permitting the extremity to hang from the edge of the table, enabled us by deeply invaginating the abdominal wall to feel a resistant body resembling the femoral head on the right side just above Poupart's ligament. This resistance could be made to appear and disappear by simply extending and flexing the thigh. In view, however, of the uncertainty of diagnosis, further efforts to correct the deformity were abandoned till accurate knowledge of the true condition could be obtained.

A few days later an *x-ray* picture was taken, and showed the

condition to be a fracture of the acetabular floor, through which the femoral head projected. The lines of the acetabular fracture could not be made out, but owing to the position of the femoral head, the freedom with which practically all the motions of the thigh could be executed, justified the belief that the entire floor of the socket was punched out (Fig. 1). After carefully studying the x-ray plate, it was deemed best to again anesthetize the patient

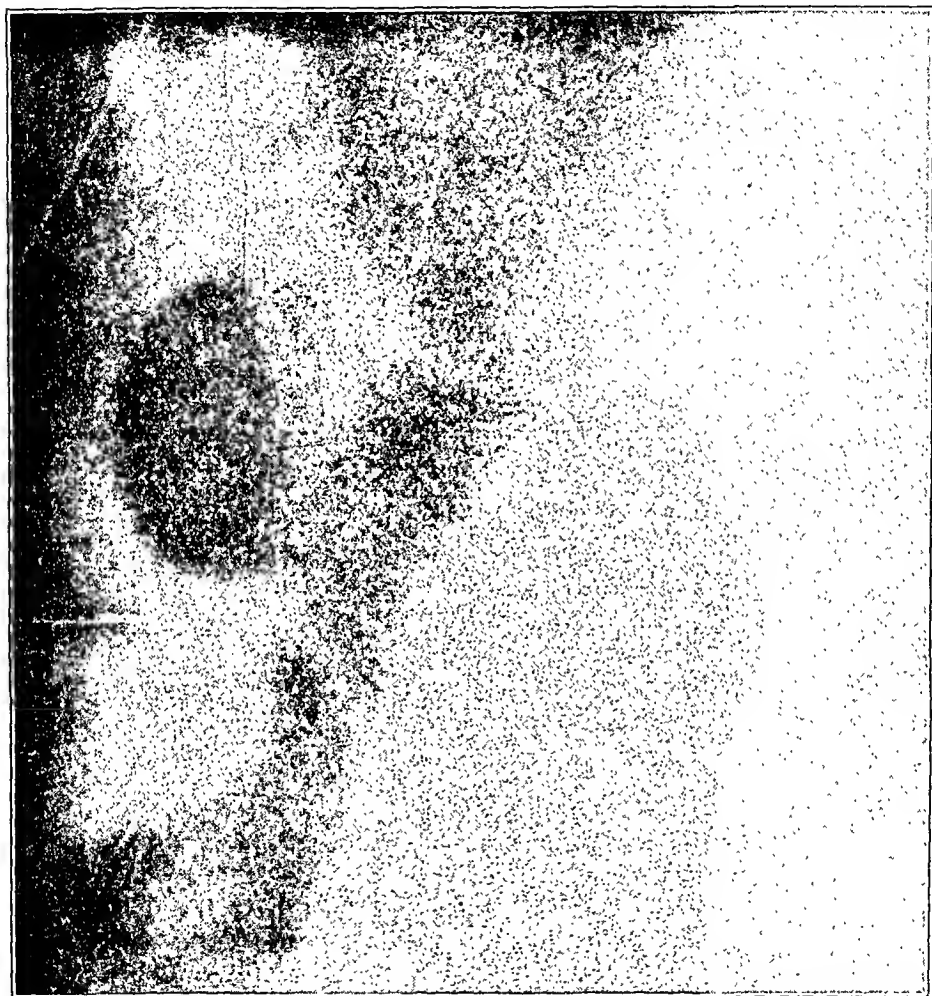


FIG. 1.—Radiogram, slightly retouched, to show the condition of an unreduced acetabular fracture. (Author's case.)

and renew the effort at correcting the deformity by bringing the femoral head out of the pelvic cavity and readjusting, in so far as possible, any of the broken fragments of the acetabulum.

The patient, deeply anesthetized, was placed on a firm operating table, and our combined efforts to replace the femoral head within the acetabular cavity resulted in a complete failure. Advantage was taken of every contingency that could have hindered the reduction, but at the end of each and every effort the trochanter major

of the injured leg remained deeply located, and the foot resumed the same slightly everted position. Finally, the patient was lifted from the table and placed on the floor; a strong, wide bandage was placed around the thigh of the injured side and the leg brought straight up at right angle to the body. In this direction prolonged and vigorous traction was made, while like traction was made laterally on the bandage applied to the thigh. This manœuvre,



FIG. 2.—Radiogram, slightly retouched, to show the condition of a successfully reduced acetabular fracture, one year after the accident. (Author's case.)

after a few trials, reduced the dislocated head of the femur, accompanying which was a sensation imparted to the hand like that frequently obtained in the reduction of a dislocated shoulder-joint. The leg now was brought down parallel with its fellow; the trochanter major appeared and could be felt just beneath the skin; the leg was of proper length, and the foot was no longer everted.

Although the leg and foot showed only slight inclination to return to the position in which we found it, it was deemed best

to apply some fixation apparatus, and accordingly use was made of extension and counterextension for one week. At the end of that time, a plaster-of-Paris cast encircling the pelvis and thigh to the knee was placed on, in which position it remained for five weeks, at the end of which time the patient was able to get around fairly well by the aid of crutches. The leg is now a little shorter than normal; motion is about perfect in all directions. The patient



FIG. 3.—Radiogram, slightly retouched, to show the condition of an unreduced acetabular fracture eight months after the accident. (Dr. Schiller's case.)

is back at the same employment doing a man's work; he walks without a limp, and the result both anatomically and functionally is most satisfactory (Fig. 2).

CASE II.—Dr. Helioder Schiller's case was that of a street car conductor, aged twenty-eight years, who fell from a car, striking the ground upon his hip. He suffered no shock, but had great pain in the region of the hip, and was not able to rise from the ground. The history shows that following the injury this man

had blood in the feces and urine, and had to be catheterized for one week. The diagnosis was that of contusion of the hip, and the subsequent treatment was instituted and carried out accordingly. The convalescence was slow and unsatisfactory, and at the end of eleven months the correct diagnosis was made by Dr. Schiller, who saw the patient for the first time. The *x*-ray taken at that time showed the condition unmistakably, and is the truest type of acetabular fracture I have yet seen (Fig. 3).

Dr. Schiller's report on the condition at present shows flexion of the leg, abduction, outward rotation, in which position ankylosis is fairly marked. There is atrophy of all the muscles of the extremity, and the patient is practically a cripple.

ETIOLOGY AND MECHANISM. The mechanism of fractures in general is subject to the widest variation and, as usually set forth, notably lacking in clearness and completeness. Normal bones may be so massive and strong, and so protected by other anatomical structures, that great violence will prove insufficient to fracture them. On the other hand, a bone may be the seat of moderate or advanced grades of one or more well-known pathological processes which so attenuate and weaken it that *slight* trauma will determine a fracture. Again, there are apparently normal bones which are so thin and frail that the resistance they offer to force or violence is very slight. Between these two extremes will be encountered the difficulty, if not the impossibility, of describing, with exactness, the true mechanism of most fractures.

Violence, to reach the hip socket, must pass through the femur. To determine a fracture of this portion of the innominate bone, not only will the degree of violence be an essential factor, but the condition, as regards shape and quality of the acetabulum. A weakened and fragile acetabular floor from whatever cause will not more likely yield under moderate force than will a strong and massive acetabulum under great force. In other words, in studying the mechanism of any fracture, not only must the type, kind, and degree of force causing the fracture be understood, but the normal strength and "mechanical capabilities" of the bone itself must be understood.

Fractures of the pelvic bones are usually due to crushing injuries, as by heavy weights passing over the body or by rolling the body between moving objects. Other forms of violence may, however, produce a fracture of these bones, as shown in the cases reported. Fractures of the acetabulum may complicate other pelvic fractures by this same kind of violence or force, but in fractures limited to this socket alone indirect force is, without question, the cause of the injury. The degree of injury to the soft parts accompanying this fracture dislocation varies within wide limits, and does not, perhaps, *always* bear a definite ratio to the death rate. Bryant reports a case in which, as a complication, a foot of the colon, the

uterus, and urinary bladder were all in view through a large perineal tear, and yet the patient lived. Wilms² and Sands,³ on the other hand, have reported cases in which death speedily occurred in the absence of symptoms indicative of serious complications. Fractures of the acetabulum with intrapelvic displacement of the femoral head were formerly thought to be due to force directly applied to the trochanter. This was an opinion expressed by many, among whom was Treves.

Fracture lines of healthy bone may pass in any direction, irrespective of the early sutures, but in unhealthy bone or in a young person the fracture lines may correspond to the original sutures, as in the case of acetabular fracture reported by Hewitt Moore.⁴

Weakness in many bones is very often produced by well-known pathological states having a definite and regular symptom group; whereas this weakness or lowered resistance is due sometimes to changes not attributable to any of these diseases, but to conditions the nature of which are as yet without explanation. This alteration of the texture of bone, sometimes designated "idiopathic fragility," appears to be a nutritional disturbance, and doubtless is responsible for many spontaneous fractures, as well as a potent element in many fractures produced by violence. The relationship between the degree of solidity, or inherent strength of a bone, and a fracture is a close one. The density of a bone may be so increased that no ordinary violence will injure it; while rarefaction or atrophy may so lower the resistance of a bone that slight muscular action alone will fracture it.

Two cases illustrating these changes in bone recently came to my notice and are worthy of mention here. The first case was that of a skull presented at a recent meeting of the Chicago Medical Society by Dr. Dudley P. Allen, of Cleveland, Ohio. This skull was everywhere normal except the parietal bones, which were strikingly translucent, and so thin that the pressure of the fingers could have easily depressed them. The second case is that of one of the phalanges in the hand of a young lady about thirty years of age. The osseous changes in this bone, as shown by the *x*-rays, were so marked that force, too slight almost to be noticed, was sufficient to produce a fracture of the phalanx.

So close is the relation between fractures and these changes, whatever they may be, that all such injuries resulting from trivial or slight degrees of violence, or possibly in unusual fractures with greater degrees of violence, should be regarded as possibly belonging to this class. It may be worthy of mention that efforts have been made by several observers, as quoted by Tillmans and others, to found the etiology of fractures on a physical basis by studying

² Deut. Ztschr. f. Chir., lxxi, 71.

³ New York Med. Record, 1877, p. 93.

⁴ Med.-Chir. Trans., xxxiv, 107.

the mechanical capabilities of bone. The great strength of the pelvic bones, their peculiar and powerful articulations and liberal muscular supply, as pointed out by Holmes, are factors which, singly and combined, contribute much to the neutralization of all forms of direct violence exerted on this portion of the body.

Our knowledge of acetabular fracture had its beginning in 1778, through a description by Henricus Callison, and since that time less than 50 cases have been reported. Arregger,⁵ in 1907, collected all the cases to be found in the literature, numbering at that time about 40. Notwithstanding the number of cases reported and the knowledge possessed regarding fractures in general, many desirable and important facts pertaining to the mechanism of this injury, as well as to its diagnosis and treatment, will not be understood till our experience with it has been considerably increased. It is necessary to consider this complicated injury as a single one, because the dislocation cannot occur without the fracture, and it is doubtful if the fracture often occurs without the dislocation.

In studying the mechanism of central dislocation of the femoral head, Katz⁶ compared it to the jamming of a hammer over its handle by striking the end of the latter with great violence. The effect of this little manœuvre is familiar to everyone, and explains possibly the acetabular fractures produced by indirect force acting through the femur with the leg in abduction, or by force through the trochanter regardless of position. It is also interesting to note that Virevaux experimentally produced acetabular fracture by violence through the femur without abducting or adducting this bone. Krönlein reported a case in which a fall upon the feet drove both femoral heads through the acetabula into the pelvic cavity.

By examining a large number of skeletons it will at once become plain how moderate degrees of force may in some instances drive in the floor of the acetabulum, as this is a partition of bone exceedingly thin. Its thinnest, or pelvic portion is at its lowest part, which would necessarily receive the highest degree of force should the latter be applied with the leg in abduction. The upper and posterior portion of the acetabulum is massive and strong, and probably would not yield under violence which ordinarily fractures the femoral shaft or its neck. It seems, therefore, important, as Schroeder has so aptly pointed out, that we should lay great stress on the relation, as regards position, between the acetabular cavity and the head and neck of the femur at the time of the injury. Some skeletons present a remarkably thin and weak acetabular floor, especially near the pubic portion, and slight force acting through the femoral shaft or the trochanter, with the leg in abduction, will suffice to drive the femoral head into the pelvic cavity. It seems difficult, if not impossible, for the acetabulum to give way

⁵ Deut. Ztschr. f. Chir., lxxi.

⁶ Beiträge zur klin. Chir., xxxii, 499.

under any circumstances except by force from without; and as this is possible only by force applied to the femur, we look upon the fracture under discussion as having its causation in indirect force and by this alone.

Muscular force as a factor in the dislocation of the femoral head after the acetabulum is fractured is important; it is far greater and much more difficult to overcome than is at first imagined, as is shown by (a) recalling the great size and number of muscles concerned, and (b) the failures which have followed the surgeon's efforts in attempting to overcome the power exerted by their contraction; this proving in some cases so difficult in the treatment of this lesion that no contrivance or method proved sufficient in withholding the femoral head from the pelvic cavity. Schloffer,⁷ in a report of a case, shows the influence of muscular contraction in this injury by taking two skiagraphs five days apart. The first picture, taken shortly after the accident, showed the fracture of the acetabulum without dislocation of the femoral head; the second skiagraph showed the femoral head well within the pelvic cavity.

SYMPTOMS AND DIAGNOSIS. The symptoms and signs of central dislocation of the head of the femur may be wanting. It was so in a case reported by Adams⁸, and one by Sands. In the latter's case the limb was capable of rotation; there was no crepitus, no eversion of the foot, no shortening of the leg. Patients after the accident have been known to walk a considerable distance with comparatively little discomfort.

On the other hand, such evidence as a deeply sunken trochanter, slight shortening of the leg with eversion of the foot, the absence of crepitus with the presence of practically all motions, although painful and limited, the evidence sometimes obtainable by rectal examination coupled with an exact history of the accident, will oftentimes justify a diagnosis without an x-ray picture. The absence of crepitus, as often mentioned, and as was true in our own case, is explained, I think, by the separation of the bone pieces by the head and neck of the femur as by a wedge, thus preventing the broken bones coming in contact.

The degree of motion in the injured leg will depend on the size and shape of the acetabular opening; if the opening is small, movements of the leg will be greatly restricted; whereas in a large and free opening the motions of the thigh will be much more free. The position of the foot may be inverted or everted, and is often due, as in many other fractures of the leg, to the direction of the force which caused the injury; although, in the words of one writer, the position is sometimes in obedience to circumstances not always easily explained.

⁷ Archiv f. klin. Chir., lxxxiv, 499.

⁸ Boston Med. and Surg. Jour., 1907, vii, 432.

From impacted fractures of the femoral neck central dislocation of the femoral head may be differentiated by the age of the patient and the comparatively high degree of injury in the latter instance. The remarkably sunken appearance of the greater trochanter and its slightly altered relation to Nélaton's line are points which distinguish the dislocation.

The certainty with which the femoral head may be palpated in either of the anterior dislocations of the femur, and its increase in length in the thyroid dislocation, will serve to differentiate any one of these dislocations from a central one.

In the dorsal dislocation, especially the one above the obturator internus tendon, the trochanter is far above Nélaton's line, the thigh is adducted, flexed, and the axis of the dislocated femur crosses the lower end of the opposite one. Moreover, in the simple dislocation all movements will be less free than when the head and neck occupy a central position.

It is not intended that the symptoms of acetabular fracture as here given are to in the least minimize the importance of the radiograph, but that each and every manifestation of all hip injuries of whatever nature should be carefully and cautiously considered. In no instance should the clinical findings settle the diagnosis, as they are frequently misleading, and the conclusions based thereon should invariably be corroborated by the röntgenologist.

MORTALITY. The mortality in this accident hitherto shown is very high, but is not due to the fracture or dislocation directly, but to the associated injuries suffered by the pelvic organs and the bloodvessels. Katz reported 11 cases of intrapelvic dislocation of the femoral head, and of this number, 6 died within a week. Arreger reported 33 cases, and 16 of this number did not recover, the majority dying within a week. In this collection of 33 cases the correct diagnosis was made in 6 cases only. No attempt has been made in this paper to tabulate the number of central dislocations now in the literature, because many of the cases have been reported on clinical data only.

Worner⁹ in 1907, collected all the cases from the literature then to be found, and out of the total number of 41 cases, 25 were rejected because neither x-ray examinations were made nor anatomical specimens obtained to substantiate the clinical diagnosis.

PROGNOSIS AND TREATMENT. The prognosis in uncomplicated cases seems favorable. This depends, however, on a correct interpretation of the injury and the employment of such means as will withdraw and withhold the femoral head from the pelvic cavity.

Complicated cases in which there is a bladder injury, an intestinal tear, or serious injury to important bloodvessels have neces-

⁹ Beiträge zur klin Chir., lii, 185.

sarily issues more difficult to forecast, and in spite of the best treatment, the prognosis is exceedingly grave. When these cases are unrecognized and untreated Nature may, in a measure, compensate for the injury by providing a semibony socket for the femoral head in its new location, which may be sufficient to subsequently bear the body weight.

In the treatment of this rare and unusual injury attention should be, as in all other fractures, directed first, toward the extent of the damaged pelvic organs. To overlook one of these complications for any length of time would obviate the necessity of planning means to reduce the dislocation or treat the fracture. The control of hemorrhage, the prompt repair of the bladder, urethra, or intestines, are important and pressing matters demanding a high degree of surgical interference which should be executed with the least possible delay.

The necessary treatment for returning the head of the femur to the acetabulum and there maintaining it can scarcely be put into words. If the entire acetabular floor is crushed in and there is free play of the femoral head through this opening, the only obstacle to overcome is the contractile force of the numerous and important muscles. The muscular force to be overcome under these conditions is much greater than that encountered in the treatment of any other known fracture. Failure has followed efforts in this direction in more than one instance.

Steps as carried out in our case may prove of value in bringing the head out and into the acetabulum, but it is stating it correctly to say that two cases would not likely be so nearly the same. If the head can be delivered into the acetabular socket by whatever means, certain exaggerated positions of the extremity, instead of great traction force, would appear to better serve the purpose of retaining the femoral head in the acetabulum. If it be remembered that Kusmin's experiments showed that this dislocation could be produced only with the leg slightly abducted, and that many cases on the living, including our own, were produced with the leg slightly abducted, it would appear that an exaggerated abducted or adducted position of the femur after reducing the dislocation would necessarily maintain the femoral head in the desired position for a sufficient length of time. Whether resection of the femoral head should be done in view of failure to keep it in the acetabulum, as advised by some, is open to question.

It is plainly a condition calling for some ingenuity and skill on the surgeon's part, especially in the management of difficult cases. As Cotton has said, it calls for more individualizing in the treatment. Many surgeons have had no experience with this condition and those who have had are cautious in their recommendations regarding methods of operation and treatment.

Extension and counterextension with lateral traction, from the

upper third of the femur, will doubtless, in many difficult cases, prevent the return of the head to the pelvic cavity. On the other hand, cases may be met with in which only a slight degree of extension may be called for.

In cases of failure to replace the head of the femur within the acetabulum, operative interference may offer the only hope of satisfactorily dealing with such a condition; but the particular type of operation, and the advantages to be gained by it, will depend much upon features opposing the reduction.

Measures of a radical nature must of necessity be viewed with much skepticism, as the indications calling for this kind of interference are difficult, if not impossible, to understand. Efficient operative measures in acetabular fractures, except for the repair of injuries to the pelvic viscera, have yet to be described, and must, therefore, if indicated at all, depend entirely upon a clear understanding of the true nature of the injury, and knowledge of such measures as will overcome any and all obstacles to its correction.

CONGENITAL SYPHILIS OF THE HEART.

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THE purpose of this paper is to show that there exists an especial form of interstitial myocarditis, localized or diffuse, due to the presence of the *Spirochæta pallida*, and resulting from congenital infection. This form of myocarditis may exist independently of any other signs or symptoms of congenital syphilis—in fact, it may be the only pathological condition attributable to syphilis that can be demonstrated at autopsy in the body of the patient; or other lesions of congenital syphilis may be associated with it. Secondly, this form of syphilitic disease of the heart is an important cause of asphyxia neonatorum and unexplained sudden death in early life; and some of the cases prove that it may cause cardiac weakness in childhood and youth, forming an anlage upon which subsequent infections (streptococcic particularly) produce valvular lesions. Further, the condition may be associated with infantilism, hypoplastic constitution or less severe grades of underdevelopment. Finally, it may lead also to the production later in life of fibroid heart and coronary sclerosis, with the complications and sequelæ incident to these conditions.

The material upon which these conclusions are based consisted of autopsy material of 12 cases furnished in part by the clinics of the

University Hospitals, and in part from the private practice of Ann Arbor and Detroit colleagues. Without giving a detailed description of each of these cases, they may be divided into three groups according to the age of the patient: (1) Cases occurring in infancy; (2) in childhood, and (3) after the age of puberty. Three-fourths of the cases fall into the first two classes—infancy and early childhood. Of these 9 cases only 1 had been diagnosticated as congenital syphilis before death. The others all came to autopsy that the problem of an undiagnosticated condition and unexplained death might be solved. Of the 3 cases occurring after the age of puberty (ages fifteen, eighteen, and twenty-two years), all had an old history of cardiac disease, and all showed decided underdevelopment, one a girl, aged eighteen years, presenting a marked condition of infantilism. The oldest case was a young woman student giving a history of having been a "blue baby," and having from birth suffered from cardiac disturbance. Death took place from a streptococcus—endocarditis and septicemia engrafted upon an older interstitial myocarditis. Her father was in the late stages of locomotor ataxia. A clinical history of congenital syphilis was obtained in the other 2 cases after the diagnosis had been made pathologically.

My share in these cases having been wholly from the pathological side, it is not necessary to go further into the clinical history than the main points given above, which may be briefly stated as follows: Only in the older cases was there a definite history of cardiac affection, and in none of the cases was syphilis considered by the clinician as having anything to do with the clinical symptoms and termination of the case. Only in 1 case was congenital syphilis positively diagnosticated clinically, and in this case no affection of the heart was suspected, although at autopsy this organ showed the most severe interstitial myocarditis, with the greatest number of spirochetes present, of all the cases. For the sake of brevity, the pathological conditions may be summed up as follows:

1. *Gross Appearances.* In the majority of the early cases the heart was large and dilated; in the others, normal in size or even undersized. The heart muscle was usually pale or contained lighter areas. The walls were usually thicker than normal, the right ventricular wall in some cases being as thick as the left, justifying a diagnosis of hypertrophy from the gross appearances. The muscle seemed moister, softer, and more translucent than normal. In other hearts, aside from a dilatation of the cavities, nothing pathological was noted in the gross examination, and the condition was not discovered until microscopic examination was made. Localized patches of interstitial myocarditis can exist without causing notable changes in the gross appearances. In the older cases there was in all the gross picture of a mitral endocarditis, with insufficiency, compensatory hypertrophy, and dilatation. Nothing in the gross appearance indicated the existence of a syp-

ilitic myocarditis, and this condition was not discovered until the microscopic examination.

2. *Microscopic Appearances.* The common feature of all of these cases is the occurrence throughout the myocardium of numerous or few light-staining patches (hematoxylin and eosin or Van Gieson's), separating or replacing the muscle fibers, and made up of a fibroblastic or myxomatous tissue, having a delicate granular or fibrillar reticulum in which lie numerous cells of lymphocyte or plasma-cell type, as well as numerous large epithelioid cells with abundant pink-staining granular protoplasm and pale nuclei. The latter type of cells presents the greatest variety of size and form,

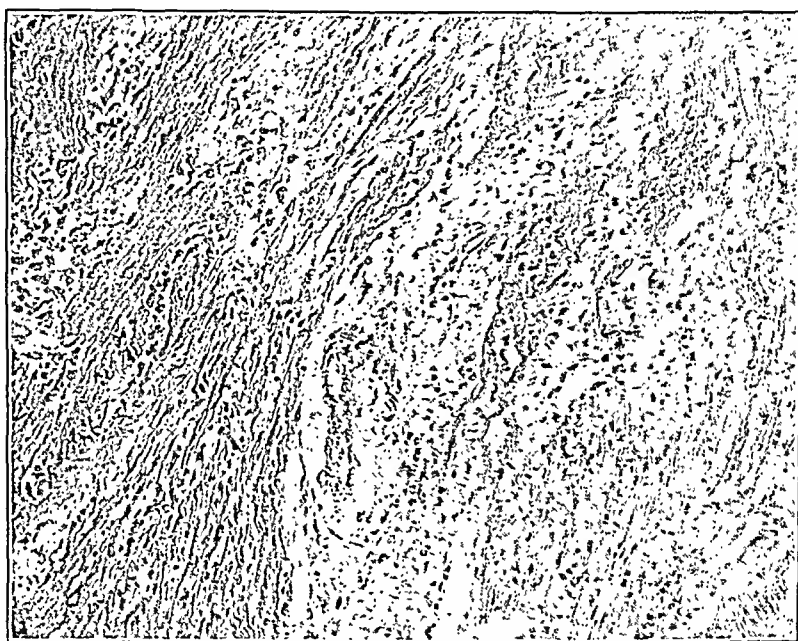


FIG. 1.—Congenital syphilis of the heart. Sudden death second week after birth. Areas of interstitial myocarditis. (Low power.)

round, oval, spindle, branched, etc. Many of these cells are vacuolated (Fig. 3); and fragmentation, with loss of nucleus, is a common feature of the larger patches. The infiltration of plasma cells and cells of the large lymphocyte type is often so marked as to catch the eye at once as a focus of small-cell infiltration. The most characteristic feature of all of these cases, however, is the light-staining, fibroblastic tissue containing peculiar degenerating cells of fibroblastic or epithelioid type (Fig. 5). The characteristics of this interstitial process are so marked and differ so much from ordinary interstitial processes that when its peculiarities are once recognized it is identified with ease.

The process does not seem to be confined to any one part of the heart wall. It may be diffuse (Fig. 2), occurring in nearly every section taken; in other cases, many blocks may be cut before a patch is found. In some cases, the left ventricular wall, or the septum, may show the most numerous patches, but in the newborn the wall of the right ventricle usually showed the most marked changes. Some blocks show the process to be most marked beneath the epicardium (Fig. 6), others show it localized beneath the endocardium. On the whole, the process seems to be more frequently localized near the epicardial surface. A striking feature of the patches is their tendency to run in narrow or broader bands between the muscle fibers.

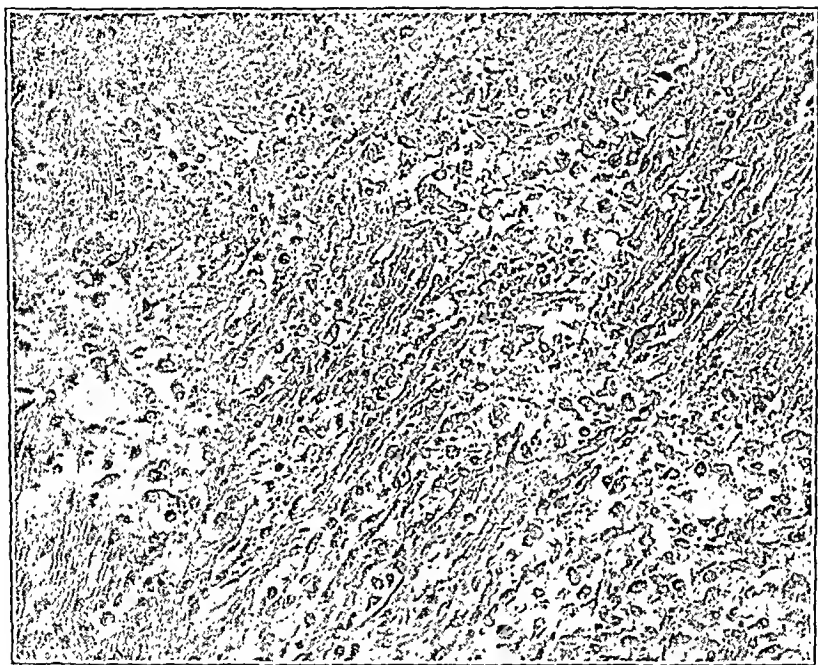


FIG. 2.—Diffuse interstitial fibroblastic proliferation. Congenital cardiac syphilis. (Higher power view.)

These bands may be of the width of 5 to 20 muscle fibers. Rarely are they large enough to be seen with the naked eye. From the larger bands smaller strands invade the neighboring muscle separating the fibrils. In sections of muscle cut transversely occasional broad bands of the light interstitial tissue cross the field (Fig. 5). Occasionally, large areas of a more diffuse process are found, the muscle fibrils appearing smaller than normal and separated by narrow strands of fine reticulum containing the large epithelioid cells, so different in size and staining and amount of cell body from the normal stroma of the heart wall.

The interstitial process seems to follow the smaller arterioles

and capillaries. It is abundant also about the medium-sized vessels (Fig. 3), less so about the larger ones, although perivascular collections of lymphocytes and plasma cells are numerous about these. The smaller vessels show an epithelioid proliferation of their walls, and the lumina are often wholly filled with cells of the same type as those of the stroma. The larger vessels, both arteries and veins, show varying degrees of thickening, the intima and the adventitia showing most prominently the result of cellular proliferation. Even in some of the newborn cases the adventitia of some of the larger vessels was markedly increased and distinctly fibroid in character (Fig. 4). Obliterating endarteritis, however, was not the common



FIG. 3.—Congenital cardiac syphilis. Perivascular fibroblastic proliferation. Neighboring heart muscle (upper left) shows marked fatty degeneration (vacuolation).

or most characteristic feature of these congenital cases, and in that respect the condition differs also from the common variety of acquired syphilis of the heart seen in adults. The most prominent feature of all of these cases is the *fibroblastic or epithelioid proliferations of the stroma along the course of the smallest vessels and apparently arising from their walls or from the perivascular tissue.*

Another striking feature of the process, as shown in all cases, is the condition of the heart muscle fibrils. Those show in the immediate neighborhood of the fibroblastic proliferations a peculiar pale coagulation-degeneration or necrosis, the protoplasm losing its striations and its ability to take the eosin stain, while the nuclei

are larger, swollen, and stain but lightly with hematoxylin. In the areas where the intermuscular proliferation is most marked and the fibrils most widely separated, bundles of pale atrophic fibrils are occasionally seen, the protoplasm of which will no longer take the eosin; and it is almost impossible to distinguish the fibrils from the surrounding epithelioid tissue except by their form and branching. Such fibrils appear to be gelatinous or partially liquefied. They still contain large, pale-staining nuclei, and there is an apparent increase of the latter. This point could not be definitely determined, as in thin sections it was practically impossible to tell



FIG. 4.—Perivascular fibroid thickening and proliferation. Marked fatty degeneration of muscle. Congenital syphilis. (Low power.)

whether the nuclei belonged to the fibrils or to the epithelioid tissue, and in thicker sections the difficulty of judgment was even greater. Fat vacuoles were common throughout the degenerated fibrils.

It must not be forgotten that in some hearts the intermuscular proliferations of the stroma are not so striking on first sight, but that to the casual observer they might be interpreted simply as an "increase of stroma," "œdema," etc., without any suspicion of their syphilitic nature being aroused. Indeed, it was only the discovery that such soft, cellular semifluid portions of the cardiac stroma contained spirochetes in great numbers that first led to their recognition as syphilitic, and furnished me, at least, with a criterion,

on the basis of which I now unhesitatingly class such charges in the heart as syphilitic beyond any question.

In all of my cases the interstitial changes outweighed in prominence the vascular ones; indeed, in some of the early cases evidences of endarteritis could be found only after some search. The older the case, the greater the involvement of the large and medium-sized bloodvessels, and the greater the frequency of occurrence of fibroid patches about the vessels or in the heart muscle. In the oldest case the soft, fibroblastic areas were found, just like those in the younger hearts, and it was from such interstitial formations that the suspicion of congenital syphilis was first entertained. The

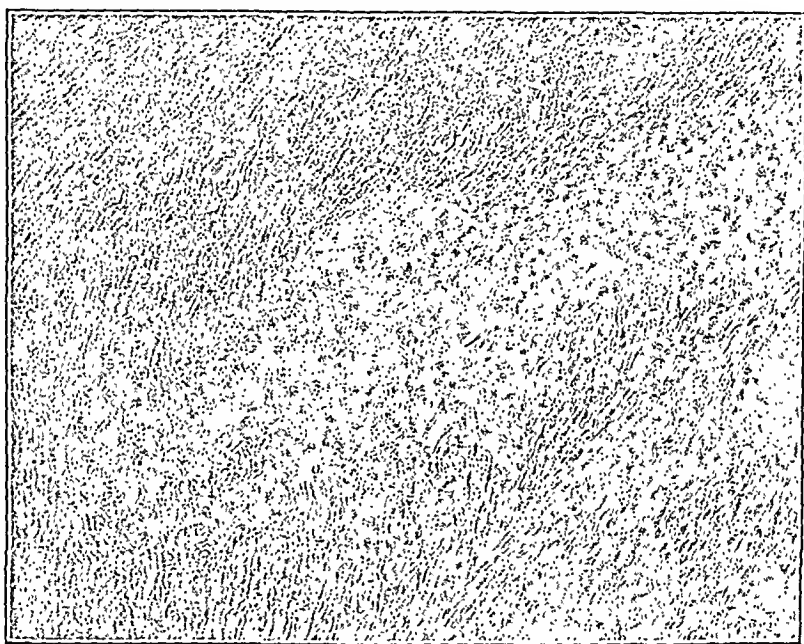


FIG. 5.—Pale, epithelioid area in heart of newborn; congenital syphilis.

occurrence of fibroid patches in the older cases in association with the fibroblastic areas and more marked vascular areas points to an age-relationship between the two conditions, although the fibroid areas may have been the result of an anemic infarction due to the obliteration of the arteries, rather than as the result of a fibroid transformation of the fibroblastic tissues. *No gumma-formation* was found in any of these cases, and the process is not identical with the gummatous myocarditis seen in late acquired syphilis. It is characterized by a much less lymphocyte and plasma-cell infiltration, and is irregularly diffuse rather than circumscribed, and there is no central caseation. Giant cells were never found. There is also no new formation of bloodvessels containing blood, although

it is possible that the fibroblastic areas may be largely made up of cells derived from the proliferating vessel walls.

Besides the peculiar pale degeneration of the muscle fibrils described above, larger areas of vacuolated muscle fibers occur in the neighborhood of the larger bloodvessels (Fig. 6). These vacuoles give the fat reaction with Sudan III and Scharlach R. In some of the newborn hearts this fatty degeneration of the heart muscle was so extensive as to account in part for the pale color and greater translucency of the heart wall. Cellular infiltration and fibroblastic proliferation were, as a rule, absent from these areas of fatty muscle. As described above, the muscle fibrils of the areas of



FIG. 6.—Area of lymphocyte-infiltration in epicardium of heart of newborn; congenital syphilis.

interstitial change showed the pale degeneration with loss of staining power and striation rather than this more marked fatty change, although often containing numerous small vacuoles.

Localized fibroblastic proliferations of the endocardium were occasionally found, the new tissue showing the same characteristics as that of the intermuscular areas. Beneath the epicardium small areas of lymphocyte and plasma-cell infiltration were common in the more severe cases (Fig. 6), and in such areas the epithelioid proliferation was not as marked as between the muscle fibrils. Fibroid thickenings (sclerotic patches) were found on both epicardium and endocardium of the older cases. Here again an age relationship is possible, but cannot be determined positively.

Of the other organs of these cases, the liver and spleen most frequently showed evidences of congenital syphilis in the form of the characteristic intralobular increase of the reticulum in the liver, and the diffuse reticular hyperplasia of the spleen. One very important point established was the occurrence of the syphilitic changes in the heart, as described above, in the absence of lesions of congenital syphilis elsewhere. Another feature of some importance is the occurrence of numerous hyaline glomerular scars in the kidneys of these cases. I have long looked upon the occurrence of hyaline glomeruli in the kidneys of the newborn as an important sign of congenital infection or intoxication—usually syphilitic. It has been

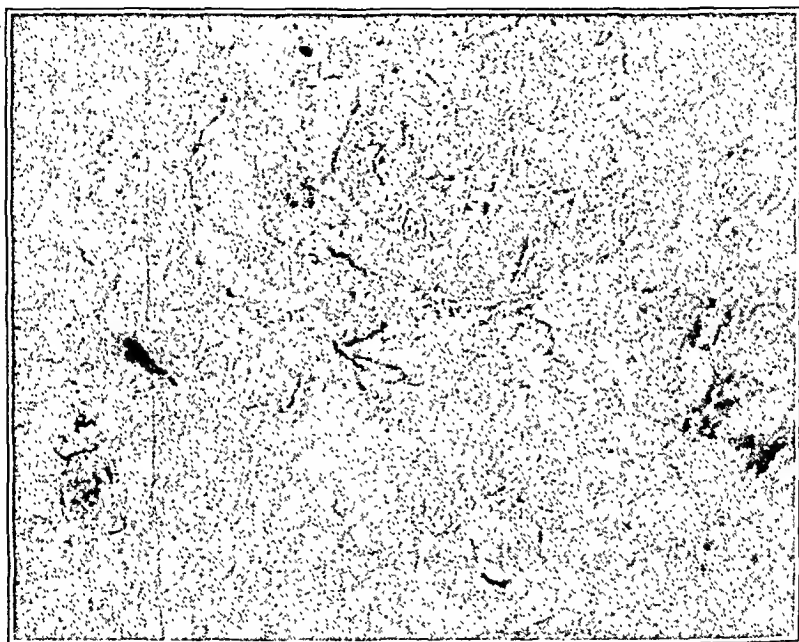


FIG. 7.—Spirochetes in area of fibroblastic proliferation. Congenital cardiac syphilis. The numerous black dots and lines represent portions of spirochetes. (About 1000+)

a common finding in all cases of congenital syphilis the kidneys of which I have examined. Syphilitic changes in the wall of the aorta and larger arteries were also found and will be reported in another article.

The proof of the syphilitic character of this form of interstitial myocarditis rested upon two points—the co-existence of typical syphilitic liver, or upon the demonstration of the presence of spirochetes. Levaditi's method was employed for this purpose. In sections so treated the fibroblastic epithelioid areas of the heart wall were found to be crowded with spirochetes (Figs. 7 and 8). They lay at every possible angle and in every direction in the soft semifluid intercellular substance, and between and upon the muscle fibrils, and

in the case of the very pale degenerated fibers apparently within the substance of the fibril (Fig. 9). In the young hearts the parasites stood out sharply and clearly revealed their distinguishing characteristics. Their number was often surprising. Every section would show great numbers cut at all planes and angles (Fig 7). Wherever the fibroblastic areas were present spirochetes were always present, usually in very large numbers. They were always more easily demonstrable in heart muscle than in liver or spleen, the coarser reticulum in the latter organs obscuring the picture more or less. For the demonstration of spirochetes within tissue I know of no material so valuable for class work as congenital syphilis of the heart.

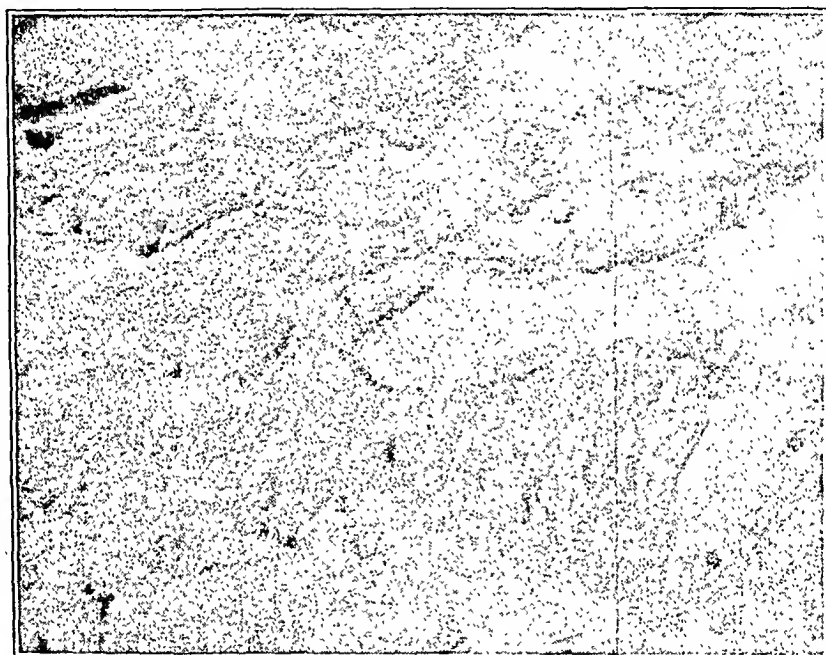


FIG. 8.—Congenital cardiac syphilis. Spirochetes in area of intermuscular fibroblastic proliferation. (About 1500+)

In the portions of the heart wall away from the areas of proliferation and pale degeneration of the muscle occasional spirochetes are found in the tissue spaces, but never so abundantly as in the pathological areas. Within the bloodvessels they are frequent. Their infrequency in the areas of marked fatty degeneration around the larger vessels makes it the more probable that this change is due to localized circulatory disturbances rather than to the localization of the spirochetes. One very important finding was the localization of spirochetes in the heart when they could not be found elsewhere.

Summing up the findings in these cases we must conclude that there exists not infrequently a characteristic form of interstitial

myocarditis due to the localization of colonies of the spirochete *pallida*, the infection being congenital in its origin. Turning to the literature on syphilis we find everywhere the statement that congenital syphilis of the heart is rare. It is only recently that the important role played by acquired syphilis in the production of cardiac disease in the adult is becoming recognized. The writers of the generation just passing away, with but few exceptions (Semola, Sachajin, etc.), considered syphilis of the heart as rare. Within recent years this view has changed so rapidly that the statement is now made that at least one-tenth up to one-third or more of all cases of heart disease are due to syphilis. In this change of view,

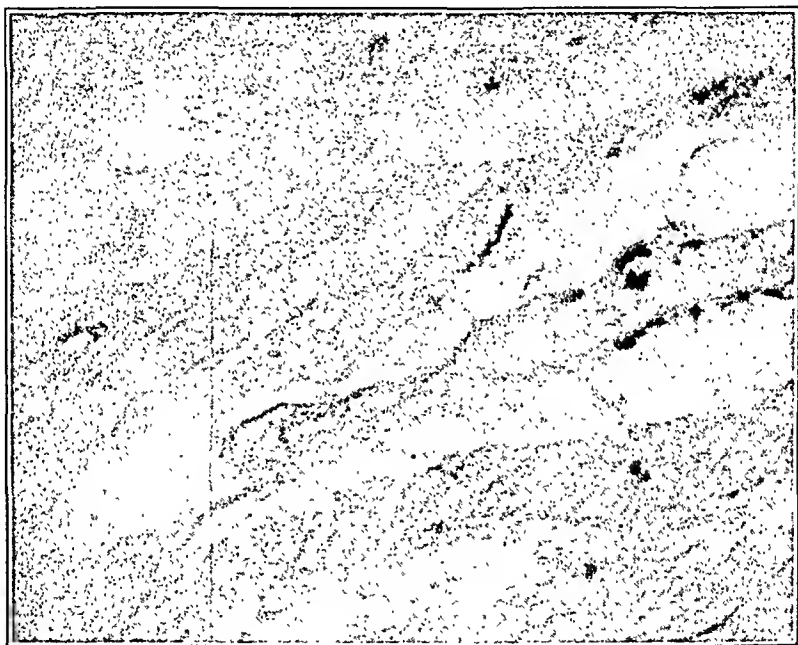


FIG. 9.—Congenital cardiac syphilis. Spirochete in or upon muscle fibril showing pale degeneration.* (About 1500+)

congenital syphilis has not been included, and the most recent chapters upon the subject still insist upon the rarity of congenital syphilis. These conclusions are based largely upon the study of heart syphilis made by Mracek¹ in 1893.

Of the 112 cases of heart syphilis collected by Mracek, only 9 were regarded as congenital; and as Hektoen has already pointed out, the syphilitic nature of some of these is doubtful. In 1 case, however, that of Coupland,² the condition was evidently that of a diffuse interstitial myocarditis. In 150 autopsy examinations of

¹ Arch. f. Derm. u. Syph., Ergänzungsheft, 1893, ii.

² Trans. Path. Soc., London, xxvii, 303.

congenital syphilis studied by Mracek, only 4 cases of cardiac syphilitic affections were found, 2 representing a nodular or gummatous form, the other 2 a most acute, diffuse, interstitial type of myocarditis. Since Mracek's study the number of reported cases of congenital cardiac syphilis has not been greatly increased. Hektoen,³ in 1896, reported a case of focal interstitial myocarditis in an infant aged six weeks. The description of intermuscular infiltration suggests strongly the same type of myocarditis as described above, but the nodular or gummatous character was marked enough to justify him in regarding it as a gummatous myocarditis due to congenital lues. Hektoen takes occasion to point out the dangerous nature of congenital syphilitic myocarditis as a possible cause of sudden death in apparently healthy children and concludes that the lesion has a clinical and practical interest of much greater weight than the interest previously accorded it as a pathological curiosity. In 1897, Guggenheimer⁴ described a rare case of fatty degeneration of the heart in a syphilitic newborn. He regarded it as a rare form of syphilitic myocarditis, different in type from the gummatous or fibroid forms. In 1898 Le Count⁵ reported a case of "gumma" of the heart in the newborn. His description of the microscopic findings agrees with that of my cases, and the condition is apparently the same, the white area seen being a large patch of diffuse interstitial myocarditis without true gumma formation.

In 1898 Adler⁶ made the most important contribution to the knowledge of congenital syphilis that has yet been given. Adler examined the hearts of four syphilitic infants, without any symptoms of cardiac disease, and dying of acute enteritis. To the naked eye the hearts appeared perfectly normal. In 2 of the cases he was unable to discover any changes that could be attributed to syphilis. In the other two hearts he found lesions regarded by him as undoubtedly syphilitic. One of these hearts showed only a localized patch of proliferating endarteritis in a small branch of the left coronary artery, at the point of greatest development almost occluding the vessel, and in the immediate neighborhood of the vessel a minute area in which the muscle fibrils were more widely separated than normal and the intermuscular spaces infiltrated with cells. The other heart showed a condition that, from the description given and from his Figs. 2, 3, and 4, is surely identical with the form of interstitial myocarditis seen in my cases. This heart was from a male child, aged three and one-half months, dying from intestinal catarrh and bronchopneumonia. The intermuscular proliferation described by Adler as occurring in this case are of the same type as in my cases; he noted the same degenerative

³ Jour. Path. and Bact., 1896, p. 472.

⁴ Inaug. Diss., Würzburg, 1897.

⁵ Jour. Amer. Med. Assoc., 1898, p. 180.

⁶ New York Med. Jour., 1898, p. 577; Trans. Assoc. Amer. Phys., 1898, vol. xiii.

changes in the muscles, and the fact that the lesions were most abundant near the epicardium. In both of these cases Adler's criterion for the diagnosis of syphilis was based upon the vascular changes, particularly the endarteritis. He regarded the intermuscular condition, however, as representing a very early state of interstitial myocarditis. Adler concludes his article by emphasizing the necessity of methodically considering syphilis as an etiological factor in heart disease.

From these few observations of congenital syphilis of the heart found in the literature, it is easily understood why all the textbooks consider it to be rare. It must be borne in mind, however, that the old criterion of diagnosis of heart syphilis, depended upon the finding of a gumma in the heart. What is really the case is the fact that *gumma of the heart is rare in congenital syphilis, but that congenital syphilis of the heart in the form of a localized or diffuse interstitial myocarditis is most probably not rare. The new criterion is the demonstration of the Spirochæte pallida in the proliferating interstitial tissues of the heart wall.* Adler could base his diagnosis of syphilis only upon the endarteritis. I have shown that the same type of interstitial myocarditis in the absence of coronary endarteritis is syphilitic, by demonstrating that these light-staining patches of proliferating stroma represent localized colonies of the spirochete and that the organism occurs in such patches in extraordinary numbers. The myocarditis described by Coupland, Hektoen, and Le Count, I believe, to be of the same type, sufficiently localized in the cases reported by the last two writers to be visible to the naked eye and to be interpreted as gummata. It is very probable that this form of congenital cardiac syphilis is not uncommon. As the cases of Adler and mine show, it may exist to a marked degree without causing any macroscopic changes in the heart hitherto regarded as syphilitic. Therefore, in all cases of cardiac disturbance in children, congenital syphilis should be carefully considered as a possible factor.

My series of cases also show that it can be a cause of asphyxia neonatorum and unexplained sudden death in infancy. Under such circumstances the possibility of congenital cardiac syphilis must be borne in mind and a thorough microscopic study of the heart carried out. The same thing is true of cases of non-development, infantilism, chronic valvular lesions in children, and young adults, etc. For all of these conditions an etiology of congenital syphilis of the heart is possible, and the diagnostic criterion is the demonstration of fibroblastic areas in the heart wall containing colonies of spirochetes.

The fatty degeneration of the myocardium described by Guggenheimer and believed by him to be due to syphilis, deserves mention here, since all of my cases showed patches of marked fatty change. As suggested by Guggenheimer, it may be the result primarily of

the syphilitic infection, or it may be caused by it secondarily as a result of a lack of oxygen.

In conclusion, congenital syphilis of the heart occurs most frequently in the form of a diffuse interstitial myocarditis due to the presence of the *Spirochæte pallida* in large numbers, without ordinarily producing characteristic macroscopic changes so that the absence or presence of congenital cardiac syphilis can be told only by a thorough microscopic examination of the heart wall.

PERSONAL EXPERIENCES WITH THE USE OF SALVARSAN (DIOXYDIAMIDOARSENOBENZOL, OR "606") IN THE TREATMENT OF SYPHILIS.

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THE announcement less than a year ago of a discovery by Ehrlich of a new cure for syphilis created much excitement in medical as well as lay circles. The reports in the literature following the early trials of the new remedy led many to believe that the millenium had been reached so far as the treatment, and thus the cure, prevention, and eradication of that protean disease, syphilis, was concerned. By many the antispecific, mercury, was already relegated to the rank of second choices in the selection of a drug to combat the disease. Recently the pendulum has swung the other way; a sound reaction has taken place, and the new remedy, salvarsan, now bids fair to take its proper place in the list as a result of scientific study of many thousand cases of lues in all its phases. But the complex and manifold nature of the matter under investigation will necessitate the gathering and correlation of a mountain of data before a just and accurate verdict can be reached.

Through the generosity of Professor Ehrlich, salvarsan has been tried in more than 30,000 cases of syphilis in an effort to establish its real value and to determine what dangers, if any, attend its application in man. The trend of opinion from a perusal of the enormous literature on the subject, with its labyrinth of errors and exaggerations, out of which it is difficult to extricate one's self, seems to be that the drug is of inestimable value in the control of practically all the manifest lesions of the disease, but that it is not, at least in the present dosage and mode of application, a certain

cure for syphilis. It would seem, judging from our own experience and that of innumerable others, that the early hopes for a *therapia sterilisans magna* are a *pium desiderium*.

It is our purpose in the following pages to give the impressions we have gained from the observation of about fifty cases of lues treated, for the most part, in the wards of the Mount Sinai Hospital. We say "impressions," since we do not feel justified in drawing binding conclusions from the study of a comparatively small material observed for a relatively short time, especially as stated above, in a disease of so variable an aspect.

It should be stated that a complete physical examination, including an examination of the eyegrounds, was made in every case selected for the administration of the drug. The urine was carefully examined for evidence of kidney involvement. All cases with organic lesions of the heart, kidney involvement, or eye trouble referable to the optic nerve (other than those of specific origin), were rejected. After the drug was given, the patient was kept in bed for a few days, especially in the earlier cases, and in every case that ran a temperature. The latter were few in number, so that most of the patients were out of bed on the second or third day, unless kept in bed by pain following the alkaline injections. Wassermann reactions were made in all the hospital cases both before and after the injection. Blood examinations were made only in cases with temperature or complications, since our early cases showed nothing of interest in the blood picture after the drug was given.

We feel that at the present time, when the drug may be considered in its experimental stage, that every precaution should be taken to select for injection only those cases that are free of all organic ailment, and that cases debilitated by the virus of lues, which are proper ones for the drug, should be given minimal amounts of alvarsan.

RESULTS. From a study of our cases we can safely state that all manifest symptoms of syphilis yielded to the injection at least for the time being. Chancres healed within a week or two without any local treatment. Lymphadenitis was only slowly or partly affected. In the first three weeks a marked diminution in size and an increased mobility of the nodes were observed, and then the condition remained stationary, so that in some of our cases the nodes could be felt after the lapse of six weeks or longer. Of the secondary cutaneous syphilides, the macular and pustular lesions disappeared much more promptly than the papular eruptions, which often proved quite obstinate. In one of our cases the pustular eruption disappeared promptly, but two papules on the face were still present at the time of this writing, four weeks after the injection. Mucous patches and eroded papules of the mucous membrane underwent an astonishingly rapid evolution, and it is in these lesions that the remedy shows its most wonderful and magic-like effects. Even in our worst

case the pain and difficulty in swallowing disappeared within twenty-four hours. The dirty sloughy ulcerations healed in a few days—a result which we never before obtained with any of the mercurial preparations. Moist condylomata likewise promptly underwent retrogression. In most of our cases an examination for *spirochete pallida*, positive before the drug was given, twenty-four hours after the injection was negative. (This is of the utmost importance from a sociological standpoint, for with the disappearance of the infecting organism the danger of spreading the disease is minimized.) Dry papules yielded more slowly. Malignant syphilis, accompanied by fever and pain in the joints, of which we treated two cases that were refractory to mercury, was quickly healed.

Of the late specific lesions of the skin the circinate squamous syphilides reacted most quickly. A case with multiple squamous-circinate syphilides of the face and trunk which had been resistant to five thorough courses of inunctions and sixteen injections of enesol was cured by one dose of 0.7 gram salvarsan within two weeks. Cutaneous gumma responded to the treatment more slowly, requiring for an ultimate cure from three to four weeks. It is our impression that these cases could have been influenced by mercurial treatment in about the same time. In one case of gumma of the muscle the lesion was dissolved in a short time without breaking down. In this patient, who had been under our care for a long time, previous gummata had invariably broken down in spite of energetic treatment by hypodermic injections of salicylate of mercury. In the same patient a gummatous affection of the knee-joint, which for eight months had resisted this treatment and also large doses of KI internally, was absolutely cured in less than four weeks. One case of gumma of the liver where the diagnosis was substantiated by laparotomy and biopsy was apparently cured. A bilateral gummatous orchitis was beneficially influenced in so far as the swelling disappeared and the pain subsided. Periostitis and iritis were cured within a week. One of our cases with nocturnal bone pain enjoyed his first sleep in over four weeks the night after the injection. One case of hereditary lues, with chronic productive periostitis of the lower third of the leg and ankle-joint, which had resisted all previous treatment with mercury, today, ten days after the injection, is free of all pain, the swelling has disappeared, and the patient is practically well—a result which we could not achieve by any other means at our command. Gummatous ulcers and infiltrations of the nasopharynx healed within a short time. The dirtiest ulcers became clean within a few days, the crust formation ceased, the fetor disappeared, and a rapid epithelialization took place.

One case of cerebral lues was only slightly benefited. The pain in the head, which was the chief symptom at the time of the injection, was only slightly ameliorated. Another case of cerebral lues, with

diabetes insipidus, where excessive thirst was a very annoying symptom, was improved, inasmuch as the great thirst and the polyuria disappeared after the drug was given. The patient's general health was improved. Of the two cases of general paresis, one left the hospital without any visible improvement; two days after the injection he was removed to an institution to be restrained on account of his mental symptoms. The other is much better mentally than before the injection. He shows more energy, is less emotional, and takes interest in his business affairs, which he had not done before. We feel certain, however, that this result is merely temporary or coincidental. One case of tabes, who had received three injections of 0.45 gram each, at intervals of four weeks, showed marked symptomatic improvement; the Argyll-Robertson pupil disappeared, but the ataxia was uninfluenced. A case of specific pachymeningitis whose chief complaint was headache which persisted in spite of mercurial injections for years, was promptly relieved by one injection of 0.4 gram in liquid paraffine.

THE WASSERMANN REACTION. As will be seen by reference to the chart, Wassermann tests were made in forty-four of the cases. Of these, thirty-nine were positive and five negative before the drug was injected. Of the positive cases, only three were made negative, and in one of these but a few weeks have elapsed since the injection.¹ A number of the cases gave weakened reactions many weeks afterward. Reference to the chart will show that in a number of the cases the reaction became negative only to become strongly positive again. A few cases that were weakly positive before the injection showed complete inhibition after the drug was given. All the above tests were made with the same antigen extract, with ample controls.

It is not our purpose to go into a detailed analysis of the results of our serum tests at this time. So far as the results may be taken into consideration as evidence of a cure of the disease, if we accept a positive Wassermann reaction as evidence of the continued presence of the so-called specific virus in the system, we must conclude that salvarsan does not cure syphilis even though it may clear up the symptoms of the disease.

RELAPSES. In our series of cases there were five relapses. Three of these occurred in patients in the early secondary stage. One patient developed mucous patches on both tonsils about two months after the first injection. The Wassermann test had been negative after the injection but became positive again shortly before the relapsing symptoms were observed. This was one of our early cases, injected according to the method of Wechsellmann with a neutral emulsion, and developed a large slough at the site of the injection. The necrotic material was sterile but contained arsenic, and a button of

¹ Two of these cases have again become positive, although no manifest symptoms have appeared.

it, removed ten weeks after the injection, also contained a large amount of arsenic. It is thus proved that this patient did not derive the full benefit of the injected dose on account of lack of complete absorption of the drug. The second case relapsed five weeks after the first injection. The patient had received 0.45 gram of a neutral emulsion, the Wassermann reaction had become negative, and remained so until the relapse occurred. The relapsing lesions were condylomata lata about the anus, and a fissure in the corner of the mouth which contained the *Spirochæte pallida*. The third case, which had received 0.5 gram of a neutral emulsion, developed a periosteal node over the frontal bone six weeks after the injection. The fourth relapse occurred in a patient with gumma of the nasal mucous membrane and bone. This case had received 0.6 gram of an alkaline solution of salvarsan, and after the injection lost fifteen pounds in weight. Two months later a progressive ulceration of the nasal septum, with necrosis, was found, and the patient was put on injections of mercury. The fifth case relapsed three months after an injection of 0.6 gram of a neutral emulsion of salvarsan, given for mucous patches in the mouth, etc. The relapsing lesion was a squamous syphilide of the palms. The case has received a second injection.

TECHNIQUE AND MODE OF APPLICATION. In our first series of cases (sixteen in number) we employed a neutral emulsion prepared according to the method of Wechsellmann and injected subcutaneously under one of the shoulder blades. On account of the proportionately large number of indurations and necroses following this procedure, an experience in common with other observers, we soon abandoned this method. It is probably not accidental that three of the relapses that occurred were in patients treated in this way. Two of them had a local necrosis, and it is certain that the injected doses were not fully absorbed. It was found that the necrotic material obtained from the masses, and in one case the slough itself, contained arsenic many weeks after the drug was injected.

In the next series of cases we injected the patients with an alkaline solution of salvarsan prepared in the following manner: The drug was shaken in a glass cylinder containing about thirty beads with 3 to 5 c.c. of warm sterile water until a clear solution was obtained. We then added sufficient of a 15 per cent. solution of NaOH to re-dissolve the drug, after it had been congealed at the neutral point, by the gradual addition of the alkali. More recently, we have improved this technique by rubbing the drug in a small mortar with the alkali, adding the NaOH (15 per cent.) drop by drop until the drug is completely dissolved. A few drops of warm sterile water are added from time to time to facilitate the rubbing. The amount of a 15 per cent. solution of NaOH necessary to completely dissolve 0.6 gram of salvarsan will be found to vary between 1 c.c. and 1.2 c.c., and sufficient water is then added to bring the total volume to be

injected up to between 6 and 8 c.c. (The injection is given intramuscularly.)

Quite recently we have been using the method of Kromayer in selected cases. The drug is rubbed up in a mortar with sterile liquid paraffine; a 10 per cent. suspension being made. Other oils, such as sesame oil, or, as recently suggested, a mixture of iodipin² and lanolin may be used as a vehicle. The patients are injected on alternate days with fractional doses of the drug until the full amount is given. The whole amount may be given in one injection in one or two sites. The injection is given into the buttock. It is our experience that while the effects of the drug on the various lesions manifest themselves somewhat more slowly, the end-results obtained are probably just as good as by the more rapid methods, and the pain following the injection is usually insignificant. In these cases it is not necessary for the patient to remain in bed.

In our early cases it was our practice to give to women a dose of 0.45 gram, and to men 0.5 gram, of salvarsan. We have gradually increased the dosage until at the present time we give to women a maximal dose of 0.6 gram and to men 0.7 gram. In certain individuals it was necessary to repeat the injection, and thus in some cases as much as 1.35 grams of the drug were given to a patient. It is common practice with the Kromayer method to give divided doses, aggregating 1 gram to a patient. In the majority of the cases the injection was given into the glutæus muscle; in a smaller number, into the ileo-costalis.

The intravenous method we have employed only once in the above series, and then according to the method of Schreiber. The drug was prepared as for an alkaline injection and mixed with 200 c.c. of physiological salt solution. The whole amount was then passed through a sterile filter. The injection was made into a vein at the bend of the elbow and was preceded and followed by the passing of warm sterile salt solution into the vein. The injected solution was kept at body temperature. In this as well as in all the above procedures absolute asepsis was observed in the preparation and injection of the various solutions.

We desire at this point to draw attention to the fact that the degree of pain following the injection was found to vary with the method used. The neutral emulsion caused practically no pain, but occasionally was quite painful a few days after the injection was given. However, on account of the number of necroses following this method of procedure, as above mentioned, it had to be abandoned. The alkaline injections are followed by a great deal of pain, which comes on almost immediately, requiring in a large number of the cases the administration of opiates. The pain lasts, with more or

² For the past few weeks we have been injecting the drug rubbed up in 20 per cent. iodipin. A total of 3 to 4 grams (for 0.6 salvarsan) is injected into the buttock. This method is absolutely painless, and up to date, no after-effects have been noted.

less intensity, from twelve hours up to a week or even longer. Frequently the pain subsides soon after the injection, only to return with increased intensity within twenty to forty-eight hours. The injection of the paraffin emulsion in small doses did not cause any more inconvenience in our cases than an injection with an insoluble mercury salt.

COMPLICATIONS. Our first and only case injected with salvarsan intravenously died two weeks after the injection of acute mania. Unfortunately an autopsy could not be obtained, and we are at a loss for an explanation of the cause of death. Inasmuch as there were no manifest symptoms of arsenical poisoning, and in view of the fact that the patient was addicted to the excessive use of alcohol (he had been on a spree five days after the injection of the drug, immediately preceding his re-admission to the hospital in an irrational condition), we are loth to ascribe the fatal issue to the drug.

In our first series of cases, in which the drug was injected subcutaneously in a neutral emulsion, we observed six necroses at the site of injection. In the subsequent injections this accident was not a factor.

The Herxheimer reaction (an intensity in the number and prominence of color of the skin lesions) was frequently observed. It occurred a day or two after the injection of the drug and was of very short duration. An erythematous eruption all over the body was found in two cases. Herpes zoster was observed in one case, and a small herpes labialis in another. In none of the cases was there observed any serious disturbance of the eyes or kidneys. In one case dimness of vision in one eye was noted a few days after an injection of a neutral emulsion, but this was ephemeral. In a few cases a few hyaline casts were found in the urine after the injection, but quickly disappeared.

A rise of temperature took place in a considerable number of cases. In one of these the temperature rose above 105° and was accompanied by severe chills and a follicular tonsillitis. In a majority of the cases with fever after the injection the temperature rose to 100° to 102° and remained between these points for a day or two, gradually coming down to normal. A moderate leukocytosis accompanied the rise of temperature.

In three cases diarrhoea was noted a week or two after the injection, but the majority of the cases were constipated after the injection. Irregularities of pulse or heart action were not noted in any of the cases.

CONCLUSIONS. As we stated in our introductory remarks it is not our purpose at this time to draw definite and binding conclusions. We believe that further study and much more experience are essential to a determination of the proper place to be accorded salvarsan as an antispetic. At the present moment, therefore, we do not feel that we can lay down definite principles by which the general prac-

itioner can be guided in the treatment of syphilis with the new remedy.

A study of our results, which, on the whole, are comparable with those of other reporters, will show the nature of the drug as a therapeutic agent. The indications for the use of salvarsan cannot be absolutely formulated, but we believe that fresh cases of syphilis should be given the benefit of treatment with "606," provided there are no contraindications. Cases of malignant lues, those refractory to mercury or having an idiosyncrasy to it, and patients with gummata of vital and important structures, where a rapid dissolution of the lesion is necessary to save life or prevent marked destruction of tissue, are proper cases for the use of salvarsan.

We cannot at the present time subscribe to the dictum of certain writers that every case of lues with a positive Wassermann, but without manifest symptoms of the disease, should be given salvarsan, especially in view of the fact that a large percentage of the cases treated with the drug persist in giving a positive Wassermann reaction months after the lesions have disappeared.

The idea of a *therapia sterilisans magna*, which, as Unna says, is a royal thought, worthy of Ehrlich, will, we fear, have to give way to a *sterilisans fractionata*. That the spirochete in the superficial lesions have been demonstrated to disappear within twenty-four hours in many cases, we can testify to, but that they can be removed from the body as a whole in one *coup*, especially with the present mode of application and dosage, we believe to be unattainable. Perhaps the method of application of salvarsan of the future will be its administration in repeated doses alone, or combined with mercury. Until it has been shown that repeated doses of salvarsan can be given with safety, it is our opinion that where the Wassermann reaction remains positive after the second injection of a full dose, mercurial treatment should be instituted, even in the absence of manifest symptoms.

Ehrlich has laid the foundation of a great structure; the building is in its early growth. Let us work without undue haste and carefully, for we builders share the responsibility with the architect. Whatever the future may bring forth we feel certain that Ehrlich, has enlarged our armamentarium against one of the greatest scourges of mankind by a strong, if not the strongest, weapon; and for this reason, if for no other, he will be known as one of the greatest benefactors of humanity.

We take this opportunity of expressing our thanks to Professor Ehrlich, who kindly provided us with a supply of the drug sufficient for the injection of the majority of the cases, and to Dr. Simon Flexner, of the Rockefeller Institute, for a number of tubes. We also wish to express our indebtedness to Dr. Emil Mayer for throat examinations and to Drs. J. Wolff and P. Fridenberg for their aid in the examination of the eyes.

REPORT OF CASES.

I. *Chancres.*

CASE I.—H. J., aged twenty-two years, was injected on December 20, 1910, with 0.6 gram of an alkaline solution of "606" for an initial lesion on the penis. The chancre was about 1.25 cm. in diameter, markedly indurated, and was accompanied by a moderate enlargement of the inguinal nodes. The *Spirochæte pallida* was found in the lesion. The Wassermann test was weakly positive. The chancre was healed on December 31, the day of his discharge; the inguinal glands were still present, but much smaller in size. The Wassermann test was now strongly positive. Spirochetes could not be demonstrated in the initial lesion twenty-four hours after the injection of the drug. On January 7 and January 12 no secondaries could be observed, but the inguinal nodes were still enlarged. The Wassermann test on January 12 was negative.

CASE II.—R. S., aged twenty-five years, seventeen days before admission to the hospital, noticed a small sore behind the corona penis in the region of the frenum. When he presented himself for examination the lesion was about the size of a lentil, slightly indurated, and covered with a crust. Examination of some serum from the sore revealed the presence of the *Spirochæte pallida*. The inguinal nodes were only slightly enlarged. Otherwise, physical examination was negative. On December 24, 1910, the patient received 0.6 gram of an alkaline solution of "606" into the right buttock. The injection was very painful for two or three days, but did not require opiates to control it. There was some stiffness, lasting about a week, after the injection of the drug. After the second day, and lasting for about a week, there was moderate induration of the site of injection, but this also subsided. Without any local treatment the small herpetic initial lesion disappeared within three days after the drug was given. On January 15 the patient was in good health; the lesion had entirely healed, and there have been no further developments in the case. The Wassermann reaction was negative on February 7, 1911.

II. *Chancres and Secondary Lesions.*

CASE III.—C. P., aged twenty-one, contracted a chancre two months ago. He was admitted to the hospital on January 6, 1911, with a hard chancre on the corona penis, a diffuse maculopapular roseola, and mucous patches upon both tonsils. The Wassermann reaction was positive. On January 6 he received 0.6 gram of an alkaline solution of "606" into both buttocks. On January 7 the

patient stated that the pain in the throat had disappeared as if by magic. On January 8 the mucous patches on the tonsils had healed and the eruption had disappeared over the greater part of the body and was present only on the hands and feet. The initial lesion was transformed into a clean, epithelializing ulcer. One day later the chancre was much smaller; the glandular enlargement was *in statu quo*. The patient gained four pounds in weight within four days. On January 13 the eruption had entirely disappeared. At the site of the chancre was a pea-sized superficial erosion. On January 20, the chancre was healed. The Wassermann reaction was weakly positive.

CASE V.—J. C., a schoolboy, aged fourteen years. Five months before admission to the hospital noticed a marked swelling under the left jaw bone. There was some difficulty in swallowing and slight pain on deglutition. The latter symptoms were present at the time of his admission to the hospital. Examination of the patient's throat revealed marked swelling and ulceration of the left tonsil, fauces, and uvula, with a few proliferative ulcers scattered over the right tonsil and adjacent pharyngeal wall. The nodes in the neck, especially in the left submaxillary region, were enlarged. The nodes of the upper, anterior cervical group were bunched together, forming a mass the size of a walnut. There was a shotty enlargement of all the nodes of the body. There was no rash upon the skin. The Wassermann test was positive, and numerous spirochetes were found in the ulcers of the throat. On September 26, 1910, the patient received 0.4 gram of a neutral emulsion of salvarsan subcutaneously in the right infrascapular region. The injection was almost painless; there was very little local reaction, and no fever. The day after the injection there was a reactive swelling about the site of the injection the size of the palm of the hand. Two days after the injection the patient volunteered the information that swallowing was much easier. The tumefaction in the throat was somewhat smaller and spirochetes could still be demonstrated. The glands in the neck were distinctly smaller. Four days after the injection the ulcers in the throat had almost entirely disappeared, the swelling was no longer perceptible, and the nodes in the neck were reduced to half their original size. A few spirochetes were found. The induration over the site of the injection was slightly larger and more tender. By the fifth day the throat was practically well, and spirochetes could no longer be found; the nodes in the neck were now discrete and reduced to about one-quarter their original size. One week after his admission the patient was discharged without manifest lesions. The induration, which was about the size of the palm of the hand, was incised one week later. It contained a custard-like necrotic material. Cultures proved sterile. This was the experience in all the cases in which necrosis occurred, and in every one the necrotic material contained arsenic. The patient

gained five pounds during his stay at the hospital. The Wassermann reaction was positive one week after his discharge, on December 19, and on January 8. Up to the latter date no relapse had occurred.

CASE X.—M. O., aged twenty years, entered the hospital with scars of an initial lesion, maculopapular syphilide, and mucous patches on the lips and on the soft palate. The *Spirochæte pallida* was found in the mucous patches and in the initial lesion. The Wassermann reaction was positive. On October 26, 0.5 gram of a neutral emulsion of "606" was injected under both scapulæ. There was severe pain after the injection, which was controlled by morphine. Two days after the injection the pain was entirely gone, the mucous patches had entirely healed, and the rash was much paler. Four days later the rash was almost entirely gone. Eighteen days later the patient again presented himself at the hospital. All the lesions were healed. The Wassermann reaction was still positive, however, but during this period of time he had gained twenty pounds in weight.

CASE XII.—G. S., aged twenty-four years, four months pregnant, entered the hospital on October 2, 1910, in a truly pitiable condition. For days she had not been able to swallow on account of mucous patches on the throat and an enormous enlargement of the right tonsil, which was ulcerated and probably the site of the initial lesion. The anus and vulva were studded with numerous condylomas, which were so painful that the patient could not sleep. There was a maculopapular eruption on the skin. Both disks and and laminæ were obscured with a slight central œdema and a mild specific central neuroretinitis. The *Spirochæte pallida* was found in the condylomas and on the tonsil. The Wassermann reaction was positive. On October 3, 0.45 gram of a neutral emulsion of "606" was injected in the right infrascapular region. Twenty-four hours after the injection the patient was absolutely free from pain in her throat. Forty-eight hours after the injection the excruciating pain in the vulva and about the anus had disappeared. The day following the injection there was a Herxheimer reaction, lasting twenty-four hours. On October 7 the ulcer of the tonsil was much cleaner and the condylomas were drying up. On October 9 the mucous patches on the buccal mucous membrane were healed; the condylomas were much smaller. The ulcer on the tonsil, which still showed a few spirochetes, was shallower and cleaner; the skin eruption was fading on the body and desquamating on the palms and soles. On October 11 examination for spirochetes was negative. On October 14 the lesions of the mucous membrane were well, the condylomas had healed, and the eruption had disappeared, with the exception of a few desquamating papules on the right palm. On October 24 the patient was well and free of all symptoms. The Wassermann reaction was negative. On November 7 the Wassermann reaction was again negative. On November 9 a relapse was

noted. About a dozen condylomas were found about the anus, but not at the site of the original lesions, the pigmented scars of which could be seen. A fissure in the right angle of the mouth contained spirochetes. On November 10, 0.6 gram of an alkaline solution of "606" was injected into the right ileocostal muscle. There was practically no pain or induration following this injection. She felt so well that she left the hospital three days after her readmission, with the condylomas drying up. She presented herself again on December 3 in excellent condition, free of all symptoms. The foetus was still viable.

CASE XVI.—F. K., aged twenty-nine years, entered the hospital on October 6 with a maculopapular syphilide, mucous patches in the mouth, and an intra-urethral chancre. Spirochetes could not be found. The Wassermann test was positive. On October 7, 1910, he received 0.6 gram of a neutral emulsion of "606" under the right scapula, which caused no pain or discomfort. The mucous patches on the tonsil disappeared after twenty-four hours. On October 15 the eruption had entirely disappeared, as had the intra-urethral chancre. The inguinal glands, which had been very large before the injection, were much smaller. After his discharge on October 15 the patient did not present himself until November 30, at which time a painful swelling was found at the site of the injection, which had not appeared until two days previously. This abscess was incised and a moderate amount of necrotic material was evacuated. It was sterile and contained arsenic. The Wasserman test was weakly positive. There were no signs or symptoms of lues except enlargement of the epitrochlear lymph nodes. On December 23 there was a small superficial necrosis about the size of a twenty-five cent piece. The Wassermann test was again positive. On February 2, 1911, the patient presented himself with a fading macular relapsing syphilide for which he received a second injection of 0.6 gram of iodipin.

III. *Secondary Lesions.*

CASE VI.—A. Y., a telephone operator, aged nineteen years, entered the hospital on September 22, 1910, with a macular syphilide, mucous patches on the right tonsil and soft palate, and condylomata lata about the anus and vulva. No initial lesion found. The Spirochæte pallida was found in the mucous patches and in the condylomas. The Wassermann reaction was positive. Ophthalmoscopic examination showed a mild specific right central neuroretinitis. On September 28, 0.4 gram of a neutral emulsion of "606" was injected under the right shoulder blade. On September 30 there was a marked painful induration at the site of the injection. The condylomas were drying up and the mucous patches were distinctly smaller. The eruption was more intense than before, constituting

a Herxheimer reaction. On October 1 the throat was practically well. The spirochetes were absent from the throat lesions, but were still present in the condylomas. On October 2 spirochetes could no longer be found; the condylomas were perfectly dry and much smaller. The patient had gained three pounds in weight. The site of injection was red and tender, and there were a few small pustules under the skin. On October 5 the condylomas were reduced to very small nodules, but the skin eruption was unchanged. By October 9 the skin eruption had disappeared, and the condylomas were entirely healed. The temperature, which was normal before the injection, rose on the second day to 99.5° , on the third day to 100° , and on several subsequent days to 100.4° , but was normal on the tenth day. The patient gained seven pounds within two weeks. Two weeks after discharge from the hospital, or four weeks after the injection, a necrosis about the size of a silver half-dollar developed about the site of the injection (which healed some two months later). The Wassermann reaction on October 28 was faintly positive. On November 1 and 7, negative, and it became positive again on December 5; but there were no symptoms of syphilis. On December 27 mucous patches were found on both tonsils, constituting a relapse. On January 2 she received 0.6 gram of an alkaline solution of salvarsan in the gluteal muscle. There was practically no pain or stiffness after the injection, and the lesions disappeared within four days. On January 15 the central neuroretinitis had disappeared. The Wassermann reaction was positive.

CASE VII.—P. E., a housewife, aged forty-five years; married twenty-two years; had five children. No history of lues was obtainable. Three months ago an eruption developed over the entire body. She was admitted to the hospital for specific iritis and a maculopapular syphilide covering the entire body. There was an eroded papule on the right ala nasæ, and a mucous patch in the corner of the mouth, in which spirochetes were found. The Wassermann test was positive. On October 8 she received an injection of 0.45 gram of a neutral emulsion of "606" under the right scapula. Eighteen hours after the injection there was noted a marked Herxheimer-Jarisch reaction. There was no local reaction, and the patient did not complain of pain over the site of the injection. Two days after the injection the Herxheimer reaction had disappeared, the rash was decidedly paler, and the mucous patches had healed. No spirochetes could be found. Three days after the injection the infection of the eye had almost entirely disappeared, the eye was no longer tender to the touch, and the headache had disappeared. On the fifth day there was no sign of iritis remaining, and on the sixth day the rash had entirely disappeared, with the exception of a few pigmented papules on the lower extremities. There was very slight induration over the site of the injection. Three weeks after the

injection the Wassermann reaction was still positive; five weeks later it was positive but weaker, with the same antigen extract. On January 21, 1911, the patient presented himself with an optic neuritis, a labyrinthian affection (tinnitus, vertigo, and diminished hearing) and facial palsy, all on the right side. The Wassermann reaction was weakly positive. It is an open question whether these lesions are specific in nature or are due to poisonous effect of the arsenical injection. We will report upon this interesting question in a later communication.

CASE VIII.—J. M., aged thirty-five years, had an initial lesion eight months ago. He entered the hospital in very poor condition, on account of difficulty and pain on swallowing; with his lips, floor of the mouth, buccal mucous membrane, pharynx, tonsils, and tongue covered with dirty mucous patches; a faded macular eruption on the body; and large ulcerating masses of condylomas about the anus. *Spirochæta pallida* was found in the mucous lesion, and the Wassermann reaction was positive. On October 25, received 0.5 gram of a neutral emulsion of "606" under the right scapula. Two days after the injection, which was almost entirely painless, the lesions in the mouth and on the lips had very much improved, so that the patient was able to swallow his food without pain. The condylomas were unchanged. After four days the condylomas began to dry up, and within nine days were entirely healed. The throat was entirely clear by this time. The patient gained nine pounds, and on his discharge from the hospital, nine days after the injection, was free from any manifest evidence of lesions, excepting a slight enlargement of the epitrochlear and inguinal glands. Three weeks after the injection the Wassermann reaction was still positive, though weaker. Two months after the drug was given, the patient was in good health, free from all specific symptoms, and had gained twenty pounds in weight. The Wassermann reaction was negative on December 24, 1910.

CASE IX.—F. K., aged twenty-five years, entered Mt. Sinai Hospital (the surgical service of Dr. A. G. Gerster) on March 7, 1910, with axillary adenitis, enlarged liver and spleen, tenderness over and rigidity of the lower cervical and upper dorsal vertebræ; tenderness over the left sacro-iliac synchondrosis, and tenderness and swelling of muscles of the forearm. Venereal history negative. Examination of blood, sputum, and a piece of muscle excised from right forearm for trichinosis was negative. The Wassermann test was positive on March 13. Treatment with mercurial inunctions was begun, and continued until April 12. On April 20 the following notes were made: "The patient has been running a septic temperature since admission, varying between 99° and 103°, regardless of medication, rest in bed, and fresh air treatment on the roof, for which no etiological factor can be found. He is today in about the same condition as on admission. About one week ago he developed

tenderness and swelling upon the inner aspect of the upper right leg; three days ago tenderness and swelling over the middle of the inner aspect of the left ulna; and yesterday a hard bony swelling, excruciatingly tender, over the sixth rib. Laryngoscopical examination shows a complete paralysis of the left recurrent nerve." During the month of May the condition of the patient grew worse; he became emaciated, weak, and complained of severe pains in the calf of the left leg. The temperature ranged between 99° and 102° . On June 7, treatment with intramuscular injections of mercury bichloride was instituted, and continued until July 30. Under this treatment a marked improvement took place; the patient became stronger, more cheerful, and complained little of the pain. The fever soon subsided, and the patient left the hospital on August 10 with ulcerating gummas on the tonsil, and a gumma on the posterior aspect of the nasopharynx. Following his discharge, the patient stated that he was well, with the exception of an occasional pain in the knee, until two weeks before readmission, on October 21, when he complained of pain in his throat, paroxysms of cough, fever, and pain along both tibiae. When Dr. Gerster saw the patient on his readmission he found a large pharyngeal gumma behind the soft palate, encroaching upon the right Eustachian tube, which seemed to be on the point of perforation, and had caused deafness. For this reason, and on account of the excruciating pain which made swallowing very difficult, he requested an immediate injection of "606." The Wassermann test was positive. On October 21, 0.6 gram of a neutral emulsion of the drug was injected in the right infrascapular region. The patient experienced very little pain. On the second day after the injection the pain in his throat had entirely subsided, and he could eat and swallow with ease. On October 28, the tumefaction had diminished to such an effect that the right Eustachian opening, which could not be seen before, was distinctly visible. On October 31 only a trace of the gumma was left and the hearing had markedly improved. On November 13 the gumma had entirely healed, and his hearing was only slightly impaired. The Wassermann test was positive. On December 3, six weeks after the injection, which had been painless until a few days before this date, a fluctuating mass was found over the injected area, painful on pressure. A small incision was made, and about half an ounce of a yellowish opaque liquid was evacuated. This was sterile and contained arsenic. On December 22 the patient was still free of all signs of lues, his general health was excellent, as evidenced by a gain in weight, a feeling of well-being, and an enormous appetite.

CASE XI.—C. S., aged thirty years, a theatrical manager, contracted a chancre upon the penis about fifteen months ago; this was followed by a rash on the face and neck. Two months later he developed enlarged glands in the neck, for which he was given a

course of thirty inunctions of mercurial ointment; the glands subsided, but a severe sore throat developed, for which he was given fourteen mercurial injections without beneficial effect. After taking a patent medicine containing mercury and potassium iodide for seven months, his throat became clear, only to recur again. He then received another course of inunctions, and mercury by the mouth also. At the present time, although his throat is clear, he has severe pain over the lower part of the right leg, which was diagnosed as syphilitic periostitis. The Wassermann reaction was positive. Before the injection of "606" the patient had severe tenderness of the lower third of the right tibia, the periosteal surface of which was slightly roughened. His general condition was poor; he looked completely worn out. On November 1, 1910, he received 0.6 gram of a neutral emulsion of "606," which was injected subcutaneously according to the method of Wechselmann under the right scapula; within twenty-four hours the tenderness over the right tibial bone had entirely disappeared, so that it was possible to strike the bone quite a hard blow without causing any pain. There was some pain after the injection of the drug, which was controlled by morphine. Strangely enough, although the patient complained of tenderness over the left side of injection for some time, only the right side showed any induration, and this was moderate in degree. Three days after the injection the patient was discharged with a somewhat improved general condition and without any pain over the site of the periostitis. The Wassermann reaction was positive ten days after his injection. On January 6, he remained absolutely well. On January 13, the Wassermann reaction was positive.

CASE XIII.—F. G., aged twenty-four years, had an initial lesion, with left inguinal adenitis, two and a half months ago. The glands had been incised. In due time the chancre was followed by a profuse pustular eruption and sores in the mouth, for which he had received six injections of bichloride of mercury without effect. He entered the hospital on November 9, 1910, in a deplorable condition. He was unable to walk on account of weakness, with severe pain in the right elbow, both knees, and calves of the legs. The temperature was 102°, his weight 112 pounds. A pustular eruption was present all over the body, with rupial crusts, mucous patches in the mouth, and the wound of the adenitis operation, seven weeks previously, still open. On the left thigh there are two circular, granulating areas, each about one inch in diameter. On November 11, 0.6 gram of an alkaline solution of "606" was injected into the right ileo-costal muscle. Very little pain followed the injection. On November 14 the pain in the extremities had entirely disappeared. The temperature was normal, the mucous patches were healed, the pustules were rapidly drying up, and the crusts falling off. On November 19 the eruption had practically healed, leaving brownish pigmented scars. The patient's weight was 125 pounds, a gain of

thirteen pounds in eleven days. He was in perfect health and able to attend to his business. The Wassermann test was still positive on December 3, when he presented himself for examination, the picture of perfect health, weighing 132 pounds. On January 1 he was free of all symptoms, and was still gaining in weight. The Wassermann reaction was faintly positive.

CASE XIV.—C. W., aged twenty-eight years, contracted a chancre, followed by secondaries, eleven months ago, for which he received twenty-seven injections of mercury salicylate. He entered the hospital on November 4 with mucous patches of the left tonsil and uvula. Spirochetes were present. The Wassermann test was positive. On October 5, 0.6 gram of a neutral emulsion of "606" was injected into the left subscapular region. Within twenty-four hours there was a marked improvement. The mucous patches disappeared on October 7, when examination for the *Spirochæte pallida* was negative. The day after the injection the patient complained of severe right frontal headache and dimness of vision in the right eye, which lasted until the following day. He was discharged cured on October 10. The Wasserman test was positive. On November 1 the Wassermann test was still positive. On November 13 the Wassermann test was still positive, but weaker; but on this day he complained of sore throat. The tonsils were uniformly enlarged, but showed no erosions. The fauces and pharynx had a peculiar glazed appearance. The patient presented himself three months after the injection with squamous palmar syphilides. The Wassermann reaction was negative. He was given a second injection of 0.6 gram in iodipin on February 4, 1911.

CASE XV.—H. B., a cigarmaker, aged twenty-five years, single, had a chancre on the penis eight months ago, followed in a few months by sore throat and mouth. These lesions have persisted up to the present time in spite of about seventy injections of a mercurial preparation, the exact nature of which the patient does not know. He never had a roseola, so far as he knows, but about three months ago a few pustules appeared upon the skin of the abdomen and have persisted up to the time of admission. The patient before the injection of "606" had numerous mucous patches on the lips and inner side of the cheeks and upon the dorsum of the tongue, and the crusted remains, about one-half inch in diameter, of a pustule upon the skin of the abdomen. The Wassermann reaction was weakly positive. The *Spirochæte pallida* was not found in the patches. On November 11 patient received 0.6 gram of alkaline solution of "606" in the right gluteal muscle, followed by severe cramp-like pain in the thigh, which was relieved by morphine. The patient slept well during the night. Eighteen hours after the injection the lesions on the dorsum of the tongue are less red and not so distinct at the margins. The buccal mucous membrane was little changed. There was little discomfort from the injection. Three

days after the injection the lesions upon the mucous membrane of the mouth had healed almost entirely, and the tongue patches were almost completely epithelialized. A slight fissure on the lip remained; this healed the following day, when the patient was discharged without visible lesions. On December 4 the Wassermann test was positive. The patient was free of symptoms and had gained three and one-half pounds in weight.

CASE XVII.—L. S., a cement worker, aged thirty-five years, single, about a year ago contracted a chancre of the penis; this was followed in about a month by a rash covering the body, which subsided after fifteen deep injections of a mercury salt. The lesions disappeared, to be succeeded by sores in the throat and on the tongue, for which ten injections were given, after which the sores disappeared. For the past few months the patient has noted sores on the inner side of the lips and has not felt well enough to work. Examination revealed mucous patches on the inner side and corners of the lips and patches on the tongue, on one of which the epithelium was piled up, resembling a leukoplakial patch. An examination of the heart, lungs, abdominal organs, eyes, etc., was entirely negative. The patient was thin, but otherwise in fairly good general condition. The Wassermann reaction was positive. On December 2 the patient received into one of the veins in the left cubital fossa 0.5 gram of "606" prepared according to the method described by Schreiber. The total volume of fluid injected was 200 c.c. The injection of the drug was preceded and followed by the injection through the cannula of normal salt solution. In beginning the injection, a few drops of the preparation escaped alongside the needle into the tissue at the bend of the elbow. Otherwise, the injection was uneventful, the patient complaining of little pain after the injection. One day after the injection the patches on the lips had already epithelialized and the tongue patches were drying up. There was moderate oedema of the arm about the site of the needle puncture. On December 4 the mucous and penis patches had entirely healed, and the tongue lesions were epithelializing progressively. The arm was still moderately swollen. The Wassermann reaction taken this day was positive. On December 5 the lesions on the tongue continued to improve, but the arm was still moderately swollen. The patient insisted on leaving the hospital on December 7, and could not be induced to stay. He was readmitted to the hospital on December 9, stating that he had celebrated his return to good health after the injection of "606" by going off on a debauch. When admitted to the hospital his arm was markedly swollen from the shoulder down to the finger-tips, and the skin was of a bright red color. The redness extended over the pectoral muscles on the left chest and half way across the scapula on the back. At the outer edge of the reddened area there were some small pin point papules, but the edges were not raised up. The temperature on the day of

admission rose to 102° F., but for the next two days fluctuated between 99° and 100°. The patient was noisy and unruly, and somewhat irrational, especially on the subject of his illness, refusing to permit much to be done for him. A physical examination, made with a great deal of difficulty, failed to reveal anything abnormal, aside from the condition of the arm. There were no urinary or cardiac symptoms. The urine showed a faint trace of albumin and a few hyaline casts. Blood counts could not be made.

December 11. The patient is maniacal. He has hallucinations of hearing and delusions of persecution. He refuses all medication and nourishment, but permits his attendants to dress and care for him otherwise. The temperature is 99° to 99.8° throughout the day. The pulse is good. The patient was catheterized at night and 450 c.c. of urine obtained. He became wildly maniacal about midnight shouting answers to the imaginary voices talking to him. The redness and œdema of the arm had lessened markedly by midnight, although the area of redness had extended slightly at the periphery across the chest. The border of the lesion is not elevated, and on the whole the condition does not impress one as being erysipelatous in nature.

December 12. The patient is maniacal throughout the day and night. He can be induced to take milk with chloral and bromide every two hours, however.

December 13. The patient is quiet at intervals, but when spoken to manifests the same mental symptoms as described above. He takes some nourishment. During the day the œdema and redness of the arm disappeared almost entirely. The veins of the arm and forearm can now be made out quite distinctly, but in the cubital fossa there is still a small tender indurated area.

December 15. For the past two days the patient has been much quieter, sleeping a good part of the time, but when awake manifests the same noisy mental state. His circulation is good. He has to be fed by the stomach tube. During the past two days the temperature has risen gradually from 100.6° to 101.8°. The arm condition has improved progressively, so that now his local condition is almost normal.

December 16. For the greater part of the day the patient has been noisy and irrational. He is quiet at intervals, recognizing his friends and for the first time in days calling for nourishment. The pulse and heart sounds are good. At midnight the patient was sleeping quietly. The pulse and respirations were normal. At 4 A.M. he woke up and became noisy and restless. At 6 A.M. he suddenly died. An autopsy was not obtainable.

(To be concluded.)

REVIEWS.

LECTURES ON NEURASTHENIA. By THOMAS DIXON SAVILL, M.D., Physician to the West End Hospital for Diseases of the Nervous System, London. Fourth edition. New York: Wm. Wood & Co., 1909.

LECTURES ON HYSTERIA. By THOMAS DIXON SAVILL, M.D., Physician to the West End Hospital for Diseases of the Nervous System, London. Pp. 262; 21 illustrations. New York: Wm. Wood & Co., 1909.

IN spite of Dr. Savill's work on neurasthenia having reached the fourth edition, it cannot be described as a satisfactory book. If it were wider in its outlook and showed a larger acquaintanceship with the views and work of modern authors on the continent of Europe and in the United States, it might serve as a useful elementary book for the general practitioner. If it displayed a grasp of the larger relations of the subject and expressed important or individual views of pathology or treatment, it might be valuable to the specialist in neurology as a declaration of the opinions and experience of a physician with special experience. But, while it declares some personal opinions, these are rather crude and curious than important, and little attention is given to the setting forth of the accepted views, and almost none to explanation or criticism of the most advanced and newest ideas. That the standpoint is wholly English may be deduced from the reasons given for the supposed increase of neurasthenia in late years: These are "at least three in number:" first, the extreme prevalence of influenza—"but this is not the principal reason; the chief reason is . . . the remarkable tendency to decay of the teeth." The third cause is "the greater pace at which we live," and there is "possibly a fourth cause," viz., "a proportionate increase in the amount of drinking." While all these may have causal influences in producing neurasthenia, they can scarcely be described as the chief causes or as operative in this order and degree in this country, and the last, with us, if present at all, is certainly rare. It is perhaps not fair to find fault with an English book for being English—but if it is to be so limited it should be called "Lectures on Neurasthenia in England."

Among the varieties of neurasthenia, that which follows operations receives more attention than usual, "postoperative neuroses,"

considering the frequency of their occurrence, having been rather unduly neglected. The section on treatment is fairly good, though wordy, like most of the rest of the book.

A fault of a different kind appears where the subject of diet is dismissed in less than three pages. Some mistakes and some omissions may be pardoned to the author for his sound and wholesome insistence on the relatively small number of cases in which the mental element is the more conspicuous and important causal factor, and for his assertion that the physical element is the more essential one in the major number of patients, and that whatever the origin of the disorder the change in the nervous system is a generalized one.

Dr. Savill's *Lectures on Hysteria* display a little more acquaintance with the work of other authors than his discourses on neurasthenia, but he has not been much influenced by them. The subtitle is "Allied Vasomotor Conditions," and thus, not satisfied with the vast inclusiveness of "hysteria," he manages to bring in a number of disorders, some definitely outside of the wide boundaries of his definition, and some very doubtfully allied to it—as migraine, urticaria, and erythromelalgia, of which last a very inadequate description is given. These are utilized to prop the hypothesis that hysteria depends in the main upon instability of the vasomotor centres, associated with emotional instability. He will admit, however, that "no single hypothesis is capable of explaining all the symptoms." The treatment chapter proclaims that bromides "still remain our sheet anchor," a statement sufficient alone to condemn any book containing it. In the same section, hydrotherapy is dismissed in thirteen lines; psychotherapy, in all forms including re-education, is disposed of in not much more space, and the rest-treatment is described as "first adopted by the late Prof. J. M. Charcot, and afterward known as the Weir-Mitchell treatment," a statement which would equally astonish the two distinguished authors named.

J. K. M.

NEURASTHENIA. By GILBERT BALLET, Professeur Agrégé à la Faculté de Médecine de Paris. Translated from the third French edition by P. CAMPBELL SMITH, M.D., Pp 408; 7 illustrations. New York: P. B. Holber, 1909.

WHILE Professor Ballet's book is better both in views and statement than that of Dr. Savill, it is still inadequate as a general treatise on neurasthenia. His outlook is wider, his knowledge of the subject more catholic, and if one were forced to choose between them, one would certainly get a better conception of neurasthenia from the French than from the English author. Still there is little that is new or original in the work, although an unusual willingness to

take all causes of neurasthenia into consideration is displayed and a laudably critical attitude toward the proclamations of the believers in the preponderance of single causes; thus the author firmly refuses to accept the theories which would attribute the neurosis wholly to alcohol, to gastric disorder, to enteroptosis, to genital or venereal troubles, to vasomotor disturbances, or to purely psychic causes. Reading these statements at the beginning inclines one to confidence in the judgments of the writer in other matters, and this is confirmed when the chapters on treatment is reached. Ballet, having already refused to accede to Dubois' untenable view of the essentially mental origin of neurasthenia, is naturally not satisfied with purely psychic treatment and is even anxious that patients shall be well fed, well bathed, well rested, or well exercised, according to their needs, without neglecting their psychic necessities for education or encouragement.

In contrast to the couple of pages which Dr. Savill bestows upon diet, Prof. Ballet requires for that division of his subject 125 pages. On this chapter, though excellent as a whole, particularly in its insistence on the importance of accurate diagnosis as bearing on dietetic treatment, some criticism may be made. In the first place, the selection of foods and the methods of administering them are not, as they stand, applicable to American conditions. Not many practitioners could tell offhand what sort of dishes "purée of lentils" or "court bouillon" are. Many of our patients would be astonished and some shocked if advised to drink at meals light beer, white or red wine; nor, with the modern views of purins before our eyes, would one be willing to advise sweetbread as a frequent food.

J. K. M.

MEDICAL DIAGNOSIS. By CHARLES LYMAN GREENE, M.D., Professor of Medicine and Head of the Department in the College of Medicine in the University of Minnesota, St. Paul. Third edition; pp. 725; 7 colored plates and 248 other illustrations. Philadelphia: P. Blakiston's Son & Co., 1910.

DR. GREENE'S manual of *Medical Diagnosis* is, in brief, a compact, succinct, and well-written compendium of existing knowledge of the subject, tinctured by the author's abundant experience. The fact that it has reached a third edition within less than three years is in itself evidence of considerable merit—merit which becomes quite apparent upon examination of the book. Therein one finds not only the essentials of physical diagnosis, but also a brief summary of clinical laboratory tests and the necessary symptomatological data requisite to a comprehensive and differential diagnosis. Not all methods of examination are mentioned; to have done so would have led only to confusion and embarrassment on the part of the student and

general practitioner, for whom the book is especially designed. But those methods that the author has found most generally useful are described in quite sufficient detail; in many places alternate methods are given, and throughout the book there is a certain dogmatism, which, although it sacrifices, to some extent, absolute accuracy, is, nevertheless, a desirable attribute in an experienced teacher. It is quite impossible to single out the several sections of the book calling for particular commendation; but one may say that those dealing with diseases of the thoracic and abdominal organs are very good. So-called "Teichmann's" disease (page 262), however, should be Reichmann's disease; and the discussion of diseases of the cardiovascular system would be more representative of present-day knowledge did it include some reference of the clinical applications of the newer physiology—normal and pathological—of the heart. In general, however, the book merits the confidence of students and junior practitioners, and even more experienced physicians may turn to it when desiring hurriedly to recall some elusive fact in medical diagnosis.

A. K.

SYMPTOMS AND THEIR INTERPRETATION. By JAMES MACKENZIE, M.D., M.R.C.P. London: Shaw & Sons, 1909.

ANY new work by a writer of Mackenzie's reputation and standing commands more than passing notice, and after reading his latest contribution from his pen, a review becomes a pleasure and not merely a duty. In the book under consideration the title is not a particularly happy one, yet it seems to be the best at hand. One proceeds but a little way in the subject matter before he perceives that not symptoms, but painful symptoms, together with the nervous phenomena accompanying these, are the ones which are being interpreted. The author calls attention to the great desirability of close study of early symptoms by the general practitioner, he himself speaking from an experience of twenty years in that capacity. In a masterly fashion he has collated this experience, and introduces a new viewpoint in diagnosis, namely, the importance of understanding the relation between disease and symptoms of a reflex nature, the latter in themselves bearing no relation to the situation of the lesion. For a thorough understanding of these reflex symptoms, the author urges concentrated study on the relationship of the nerves issuing from the spinal cord, and the following will illustrate his own intimate knowledge. He explains pain referred to portions of the body remote from the morbid process as due to the fact that in the course of development the tissues immediately covering the organ have been displaced. The testicular pain in renal colic, for instance, is due to the fact that in its journey down to the scrotum the covering of the testicle receives a twig from the

first lumbar nerve, and when the centre of this nerve in the spinal cord is stimulated, as in renal colic, the pain radiates to the testicle. In renal colic one never finds the skin of the scrotum hyperalgesic, but always the deep covering of the testicle, because the scrotum is supplied by the sacral nerve, while the ureter and testicle are supplied by lumbar nerves. This is offered as one of the many instances where an intimate anatomical knowledge is of greatest value in understanding a given case, and the book is replete with such examples. Referred pain and its relation to affections of the digestive tract, genito-urinary organs, cardiovascular system, and of the lungs and pleura, is discussed with the precision and accuracy of deduction which comes only from thorough intimacy with the subject. The book, which is not a large one, is enriched with numerous diagrams illustrating nerve distribution and the seat of pain in the disorders mentioned above. The easy style of the writer makes assimilation of knowledge scarcely perceptible in the enjoyment of the reading.

E. H. G.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College; assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics in the Jefferson Medical College, Philadelphia. Vol. IV, 1910; pp. 360; 47 illustrations. Philadelphia and New York: Lea & Febiger, 1910.

THE opening section of Volume IV of *Progressive Medicine* for 1910 is devoted to diseases of the digestive tract and allied organs, the liver, the pancreas, and the peritoneum. It comprises 128 pages, and is contributed by Ralph S. Lavenson, who discusses especially diverticula, ulcer, and carcinoma of the oesophagus, gastric analyses, ulcer and carcinoma of the stomach (in their various aspects), achylia gastrica, functional diseases of the stomach, pyloric spasm, gastropnoxis, the stomach in pulmonary tuberculosis, duodenal ulcer, appendicitis, constipation, diarrhoea, the therapeutic use of lactic acid bacilli, buttermilk, peritonitis, the value of levulosuria in the functional diagnosis of liver disease, jaundice, cirrhosis of the liver, pancreatitis, the value of Cammidge reaction, etc. John Rose Bradford devotes 17 pages to diseases of the kidneys, noting especially arterial hypertension in renal disease, albuminuria, bacillus-coli infections of the urinary tract, experimental nephritis, urinary calculi, etc. Joseph C. Bloodgood contributes a chapter of 98 pages, in which he discusses the surgery of the extremities, shock, wounds, anesthesia, operative technique, surgical infections, diseases and surgery of the bloodvessels, of the muscles, of

the nerves, of the skin, and of the bones and joints. William T. Belfield treats of diseases of the genito-urinary system in a chapter of 19 pages, devoting most attention to gonorrhœa, non-gonorrhœal urethritis, vesical tumors, conditions simulating tumors of the bladder, tumors of the kidney, the vaccine treatment of infections of the urinary tract, the relations of various ductless glands to diseases of the urinary and genital organs, etc. H. R. M. Landis contributes a practical therapeutic referendium of 71 pages, in which he makes special mention of adrenalin, agar-agar, alcohol, anaphylaxis, various sorts of serum and vaccine therapy, calcium, diet, digitalis, hexamethylenamine, lactic acid, mercury, opium, phenolphthalein, pituitary extract, scopolamine and morphine, sea water, strophanthus, tuberculin, and other drugs. The volume assuredly is what it pretends to be—a reflection of recent advances, discoveries, and improvements in medicine.

A. K.

A TEXT-BOOK ON PRACTICAL OBSTETRICS. By EGBERT H. GRANDIN, A.B., M.D., Gynecologist to the Columbus Hospital. With the collaboration of GEORGE W. JARMAN, M.D., Gynecologist to the General Memorial Hospital, and SIMON MARX, M.D., late Surgeon to the New York Maternity Hospital. Fourth edition; pp. 538; 163 illustrations. Philadelphia: F. A. Davis Company, 1909.

THIS book in an earlier edition, the third, was reviewed at length in this journal, and therefore, under ordinary circumstances, the publication of the present, fourth, edition, might well be allowed to pass with cursory comment; but in the new edition considerable change has been made in the book, and the collaboration of an additional author has been secured. In essentials the book is as before, thoroughly trustworthy and concise. The chapters upon the surgery of the puerperal state and of labor have been rewritten and the book has been brought fully abreast with the present-day thought. One of the most praiseworthy points, considering the book as a whole, is the definiteness of the teaching. This will be noted in all portions of the subject. One may differ more or less with certain statements and practices which are recommended by the authors, and in a few instances this divergence may be radical, but, in summing up the value of a work of this character, it must never be forgotten that one of its prime requisites is a certain dogmatic or arbitrary attitude, since without this its value as a practical book for use at the bedside would be lost. The authors are to be congratulated and the book is to be heartily recommended as a clear-cut statement of the methods of present-day obstetrics as interpreted by men of wide experience.

W. R. N.

ARTHRITIS DEFORMANS, COMPRISING RHEUMATOID ARTHRITIS, OSTEO-ARTHRITIS, AND SPONDYLITIS DEFORMANS. By R. LLEWELLYN JONES, M.B., London. Fellow and Member of the Council of British Balneological and Climatological Society; formerly Medical Officer Royal Mineral Water Hospital, Bath. Pp. 365; 38 illustrations. New York: William Wood & Co., 1910.

MR. LLEWELLYN JONES has written an excellent book. It is merely a summary of our knowledge, but it is such a good summary and so free from prejudice that it presents all the important views of the contemporaneous authorities. The problem of classification is solved by dividing the chronic joint diseases into two groups, to one of which he gives the name rheumatoid arthritis and to the other osteo-arthritis.

Rheumatoid arthritis is justified because of its widespread use. It includes not only the chronic but also the acute forms which most of us believe are merely exacerbations of the chronic forms. The chapter on etiology indicates the extraordinary confusion of this part of our knowledge, or perhaps it would be better to say, ignorance. However, three main suppositions may be distinguished—the infectious theory, the entrance of infection generally being in the mouth or nose; the auto-intoxication theory, due to disturbed digestion; and finally, the belief that it is a trophoneurosis. Somewhat subsidiary is the theory of some disturbance in the internal metabolism, particularly the thyroid gland, and possibly the female genitalia. Jones concludes as follows: that although “leaning toward the toxemic theory of its origin, one cannot but be sensible that our knowledge of the more intimate chemical changes involved is very vague, and forbids any pretension on our part to an exact etiology of the affection.” The clinical account is excellent. Practically nothing that is really new is brought out, but the symptoms are described consecutively and clearly, and the illustrations are quite satisfactory. One of rheumatoid arthritis associated with exophthalmic goitre is quite striking.

The chapter on treatment is quite full. He discusses the various methods, including a long illustrated section on hydrotherapy, electricity, etc. Practically he reaches the empirical conclusion that arsenic is probably the most serviceable drug in the chronic forms. He calls particular attention, however, to the extraordinary value of thyroid gland in a certain small group of cases. Surgical treatment, although encouraging, has not in his hands been of much service. The uncertainties of arthritis deformans are considerably multiplied when he discusses the conditions included under the term osteo-arthritis. Jones suggests that a more careful study of the whole body may, as in acromegaly, reveal a lesion in one or more of the ductless glands. He recognizes three chief types—Heberden's nodosities, *malum coxae senilis*, and osteo-arthritis of the knee.

In the treatment he lays great stress upon a restricted diet and particularly the elimination as far as possible of the carbohydrates and fats from the dietary. The other treatment does not differ greatly from that of rheumatoid arthritis. The section on spondylitis deformans is very full, and Jones reaches the very sensible conclusion that the distinctions drawn between the various types of this condition are purely artificial. Still's disease he regards as possibly due to a variety of infections, of which tubercle is probably one.

This brief analysis will suffice to indicate the essential lesson of the book, that an enormous amount of effort has been spent by the medical profession upon these chronic joint conditions and has been expended almost entirely in vain. Neither in the classification, in the etiology, in the pathology, nor in the treatment is there any definite knowledge or even much agreement regarding the results of experience, and in the clinical manifestations the advances in knowledge and observation have been trivial. It is to the author's credit that he has presented conditions as they are and has not attempted by the vehement advocacy of some theory or supposition to delude us into the belief that our information in any respect is more definite than is actually the case. J. S.

PATHOGENIC MICROÖRGANISMS, INCLUDING BACTERIA AND PROTOZOA: A PRACTICAL MANUAL FOR STUDENTS, PHYSICIANS, AND HEALTH OFFICERS. By WILLIAM HALLACK PARK, M.D., Professor of Bacteriology and Hygiene in the University and Bellevue Hospital Medical College, and Director of the Research Laboratory of the Department of Health of New York City; and ANNA W. WILLIAMS, M.D., Assistant Director of the Research Laboratory of the Department of Health of New York City. Fourth edition; pp. 670; 196 engravings and 8 full-page plates. New York and Philadelphia: Lea & Febiger, 1910.

THIS admirable book, filled with excellent illustrations, has, in the fourth edition, been much enlarged, and whenever it has seemed advisable or necessary the chapters have been revised. A section has also been added upon the bacteria concerned in agriculture and in some of the important fermentations. Revision and addition have also been made in the portions devoted to a discussion of the relation of bovine tuberculosis to that in man, the value of antimeningococcus serum, the use of bacterial vaccines, the etiology of anteropoliomyelitis and trachoma, and the prevention and cure of trypanosomiasis. The excellence and scope of this work is already so well known that it is only necessary to say that the present edition makes the work even more valuable than those that have preceded it. W. T. L.

THE PRACTICE OF MEDICINE. A GUIDE TO THE NATURE, DISCRIMINATION, AND MANAGEMENT OF DISEASE. By A. O. J. KELLY, A.M., M.D., Assistant Professor of Medicine in the University of Pennsylvania; Professor of the Theory and Practice of Medicine in the University of Vermont; Professor of Pathology in the Woman's Medical College of Pennsylvania, Philadelphia. Pp. 945; 23 illustrations. Philadelphia and New York: Lea & Febiger, 1910.

THE author of this *Practice of Medicine* states in his preface that his book represents an effort to prepare for the student and the junior practitioner of medicine a guide to the nature, discrimination, and management of disease that should contain the essentials unadorned with great detail. He further states that he has devoted most space and attention to the practical aspects of medicine; to the elucidation of those principles exemplified in disease at the bedside, in hospital wards and clinics, and in the consulting room; and to the clinically important and more common disorders rather than to the rarer diseases, however interesting. A systematic arrangement of the subject matter has been adopted to facilitate comprehension of the mutual relations of different clinical and pathological entities. Emphasis has been laid upon the definition of processes of disease—to impress upon the student the necessity of accuracy in his use of terms and in his clinical descriptions. Inasmuch as the final object of medicine is practice, most space has been devoted to symptomatology, diagnosis, and treatment; and to insure a rational grasp of these main objectives, they are presented in their mutual relationship by means of brief connecting sections on etiological factors, essential anatomical lesions, and pathological physiology. Throughout the book an endeavor has been made to portray the nature and natural history of disease, to correlate disturbed or perverted function with altered structure, to explain the development of symptoms, and to elucidate the sequence of cause and effect. Under the individual diseases, as a rule, at least one method of treatment has been emphasized. A few formulæ have been included—as an aid to the junior practitioner, pending the acquisition by him of experience and mature judgment. Intentional limitation of space and the primarily clinical purpose of the book made it seem desirable to the author to omit discussion of the biological characteristics of the infectious microorganisms and of the technique of laboratory methods of diagnosis.

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF
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The Blood in Hodgkin's Disease.—FABIAN (*Wien. klin. Woch.*, 1910, xxviii, 1515) has analyzed the literature on Hodgkin's disease or lymphogranulomatosis, with special references to the blood findings, with the following results: (1) The majority of the cases exhibit a polymorphonuclear neutrophile leukocytosis of medium grade. (2) The blood (including leukocytic formula) may remain unchanged. This happened in about one-fifth of the cases. (3) Throughout the disease, or as a transitory phenomenon, there may be a more or less marked leukopenia. This was observed in about one-fifth of the cases also. (4) Qualitatively, the blood often shows a relative polymorphonuclear neutrophilic leukocytosis (to 99 per cent. and more) with a corresponding diminution in lymphocytes (0 to 3 per cent.). This occurs most frequently with leukocytosis, at times with leukopenia, seldom with normal count. (5) In about 25 per cent. of cases, eosinophilia, usually of slight or moderate degree, is observed. (6) Rarely mastzellen are increased. (7) Occasionally a few myelocytes are seen. (8) In one case an enormous increase of platelets was recorded. (9) Occasionally there is a moderate, rarely a marked, lymphocytosis, which is generally transitory. (10) In the course of the disease a secondary anemia develops, mild in the earlier stages, later severe. The results show that more is to be gained from repeated examinations at intervals; a single examination is often misleading. From the few cases of lymphosarcoma reported with careful blood studies, it appears that blood changes similar to those in Hodgkin's may be found, making differential diagnosis by blood examination impossible.

A Modified Antiformin Method of Detecting Tubercle Bacilli in the Sputum.—LOEFFLER (*Deut. med. Woch.*, 1910, xxxvi, 1987) in attempt-

ing to shorten and simplify the antiformin method of detecting tubercle bacilli in the sputum has found the following modification very satisfactory: A quantity of sputum (5 to 20 c.c.) is measured and placed in a flask with an equal quantity of 50 per cent. antiformin and the mixture is boiled. Solution of the sputum occurs almost at once with the production of foam and a slight brownish color in the liquid. To 10 c.c. of the cooled solution (which is sterile) 1.5 c.c. of a mixture of 10 volumes of chloroform and 90 volumes of alcohol are added and the whole thoroughly shaken. The specimen is now centrifugalized about fifteen minutes. Chloroform is found at the bottom of the tube, and on its upper surface the sediment is found. The supernatant fluid is poured off, and with a pipette the sediment is transferred *in toto* to a glass slide. The excess of fluid is removed with blotting paper and a small drop of egg albumin (preserved with 0.5 per cent. carbolic acid) added to and mixed with the sediment, which is then spread on the slide. The specimen is air-dried and fixed in the flame. Staining is done by the Ziehl-Neelsen method, 3 per cent. HCl, alcohol being used to decolorize. As counterstain, Löffler prefers malachite green. The staining properties of tubercle bacilli are not injured in any way. The method requires fifteen to twenty minutes and has given very satisfactory results.

Ascaris Poisoning.—GOLDSCHMIDT (*Münch. med. Woch.*, 1910, lvii, 1991) describes the symptoms suffered by himself and by others of his acquaintances as a result of dissecting fresh ascaris material. The toxicity of ascaris is well known to zoölogists. There is considerable variation in individual susceptibility. Working with material a single time often leads to no symptoms. If, however, one continues to handle fresh ascarides, unpleasant effects are apt to occur and to increase in severity if the work is persisted in. In the mildest forms of poisoning there may be simply tenderness of the fingers, with or without swelling. More often there are symptoms of irritation of the respiratory tract. Sneezing is common, and there is frequently coryza with injection of the nasopharyngeal and laryngeal mucosa. Conjunctivitis is not uncommon, and may be severe if fluid from the body cavity of the worm comes in direct contact with the conjunctiva. True asthmatic attacks with dyspnoea and cough are among the usual manifestations of the poisoning. They frequently show a remarkable periodicity, coming on usually in the night or early morning hours, often waking the patient at the same hour day after day. The symptoms may persist for two weeks after cessation of contact with, or proximity to ascaris. The syndrome resembles hay fever strikingly. In those who have already suffered an attack of ascaris poisoning a hypersusceptibility seems to exist, and the symptoms may be precipitated simply by entering a room in which ascarides are being dissected. Material which has been preserved in alcohol exhibits much less toxicity than the fresh worm and to some is quite innocuous. Goldschmidt says that ascaris megaloccephala of the horse is considerably more toxic than ascaris lumbricoides of man and the hog. The nature of the toxic substance is unknown; it is possible that the peculiar, disagreeable odor of ascaris stands in close relationship to the toxin.

The Relation of the Lymphocytes to Lipolysis and Bacteriolysis.—In a previous communication BERGEL demonstrated that the lymphocytes of the spleen and lymph glands and of tuberculous exudates possess a lipolytic ferment. He now (*Münch. med. Woch.*, 1910, lvii, 1683), attempts to explain many of the lymphocytes as biological reactions, due in large measure to the presence of this ferment. Attention is called to the predominance of lymphocytes in tuberculous exudates and the occurrence oftentimes of a lymphocytosis in the blood of the tuberculous. This, Bergel believes, is to be accounted for by the presence of fat in the tubercle bacillus. Again, it is often impossible to demonstrate tubercle bacilli in caseous glands, cold abscesses, etc., by the Ziehl-Neelsen method of staining, though recent work has shown that bacilli, morphologically like tubercle bacilli, may be found in such material by Nam's stain, a fact explained, Bergel thinks, by digestion of the fat in the tubercle bacilli by lymphocytic lipose. In leprosy Bergel finds conditions analagous to those in tuberculosis. The presence of lymphocytosis in lues suggests similar conditions in this disease, since it is practically established, the author says that the syphilitic antigen contains a lipid substance. For this reason, too, he finds a causal relationship between positive Wassermann reaction and lymphocytosis. The lymphocytosis in typhoid fever and the increased lipolytic activity of the blood serum reported in this disease suggests to the writer the possibility that typhoid bacilli contain a lipid. The lymphocytosis of pernicious anemia is attributed to the hemolytic lipoids which have been demonstrated in the mucosa of the gastro-intestinal tract by Berger and Tsuehiya. The cause of lymphatic leukemia may be a lipid-containing organism. The author cites the following diseases as instances in which positive Wassermann reaction and lymphocytosis may be found co-existent: Lues, leprosy, scarlet fever, malaria, pernicious anemia, paroxysmal hemoglobinuria, pulmonary tuberculosis, trypanosomiasis, and pellagra. Other illustrations are given in the attempt to show that where increased lipolysis may be required, the biological response is an increase in the lymphocytes.

A Method of Counting Eosinophile Leukocytes.—DUNGER (*Münch. med. Woch.*, 1910, lvii, 1942) has devised a quick method of counting the absolute number of eosinophile cells in the blood. He employs the counting chamber (ruled for white count) and a white pipette, permitting a dilution of 1 to 10. The diluting fluid consists of 1 per cent. watery eosin and acetone, each, 10; distilled water, ad 100. The solution must be tightly corked and is fairly permanent. A 1 to 10 dilution of the blood is made, the mixture thoroughly shaken three to five minutes in the pipette, and a drop placed in the counting chamber. Only the eosinophile cells are well preserved. They stand out sharply as pink bodies in the pink fluid and are readily distinguished with a magnification of 120 to 150 diameters. Nine square millimeters of the counting chamber should be counted. Ordinarily 9 to 18 eosinophiles are seen in this area, the normal absolute number of these cells per c.mm. being about 100 to 200. With a little practice an increase in number is recognized at a glance. By determining the total number of leukocytes in the usual way, the percentage of eosinophiles is readily computed. The whole procedure requires but a few minutes.

Infantile Splenic Anemia Caused by Leishman's Bodies.—JEMMA (*Deut. Arch. f. klin. Med.*, 1910, c, 466) has had seven cases of infantile splenic anemia admitted to his clinic within the last year. All presented marked splenic tumor. Anemia was moderately severe in some, absent in others. The leukocytes were normal or moderately increased in number. In six of the patients splenic puncture at once gave the diagnosis; numerous Leishman bodies were found in the stained smears of splenic pulp. In the seventh case (the second in the series) repeated punctures of the spleen failed to reveal the organisms, and, therefore, two dogs were inoculated. Within three months one of the dogs, which had received an intrafemoral injection of the material obtained from the spleen, became ill. His spleen was excised under ether anesthesia (with subsequent improvement in the dog's condition), and numerous parasites were demonstrated. (Experiments of Novy and of Nicolle have shown that dogs and apes are susceptible to the infection, other laboratory animals being apparently immune.) Novy-Nicolle agar, inoculated with splenic pulp, showed growth of the organisms.

A Quick Method for the Use of Giemsa's Stain.—GIEMSA (*Münch. med. Woch.*, 1910, lvii, 2476) describes a new method of using his azur-eosin (Romanowski) staining mixture, by which the time is greatly shortened. The mixture is diluted with an equal volume of pure methyl alcohol and placed in a dropping bottle. The air-dried blood film is placed in a dry Petri dish with the specimen side up and covered with 10 to 15 drops of the staining solution for thirty seconds. Enough distilled water is poured in the dish to cover the specimen (10 to 15 c.c.) and the dish is agitated till a homogenous mixture of the stain is obtained. After three minutes the specimen is removed (five minutes are required to stain trypanosomes and spirochetes). The specimen is washed in water, dried, and mounted in balsam. It is not known how permanent the mixture of stain and alcohol is, and Giemsa, therefore, advises the preparation of small quantities at a time. Acetone may be substituted for the alcohol. The granules are much better stained, but acetone has the disadvantage of extreme volatility.

The Action of Sodium Butyrate in Young, Fasting Dogs.—MARX (*Ztschr. f. klin. Med.*, 1910, lxxi, 165) has sought to reproduce the symptoms and signs of diabetic coma in young, fasting dogs by the administration of sodium butyrate. Having attained this end, he studied the effect of carbohydrates and alkalies on the toxic animals and arrived at the following conclusions: (1) Sodium butyrate, or the products derived from it in the organism, is toxic and produces a symptom complex in young, fasting dogs similar to diabetic coma in man; its duration is short. (2) This condition may be produced regularly by intraperitoneal administration, rarely when the butyrate is given per os. (3) The transformation of the sodium butyrate into diacetic acid and acetone seems to account for the appearance of toxic symptoms. Administration of carbohydrates lessens the toxic manifestations. (4) In diabetic coma of man one has to deal, perhaps, with a specific poisoning with butyric acid and its derivatives (closely allied fatty acids) rather than with a general acid poisoning (acidosis). The poisoning

becomes evident in the dogs through irritability, somnolence, sleep, deepest coma, with anesthesia and loss of reflexes. Various stages are recognizable, though not sharply defined: (1) Stage of excitement, vomiting. (2) Somnolence. (3) Sleep. In two instances mild clonic spasms were noted. Alkalies apparently served merely as a vehicle which removed the acids more rapidly than usual. The toxic signs appear when the amount of acid formed exceeds that excreted to a certain extent. The poison has a special avidity for the central nervous system, attacking the brain and vital centres.

The Ammonia, Amino-acid, and Peptid Nitrogen in the Urine of Pregnant Women.—FALK and HESKY (*Ztschr. f. klin. Med.*, 1910, lxxi, 261) have attempted to determine whether the functional impairment of the liver in pregnancy, as shown by alimentary levulosuria, is also recognizable in the protein metabolism. (Falk and Hesky found an alimentary levulosuria after 100 grams levulose per os in 80 per cent. of their cases.) The ammonia was determined by the method of Folin-Spiro. Amino-acid and peptid nitrogen were estimated by formalin titration. Falk and Hesky conclude from their studies: (1) There is a fairly constant abnormality in the ratio of nitrogenous bodies in the urine in pregnancy. This shows itself in a relative increase in the ammonia, amino-acid, and peptid nitrogen as compared with the non-gravid state. The amino-acid nitrogen is increased in about 73 per cent., the peptid nitrogen in about 76 per cent. of cases. The increase may amount to two or three times the normal. (2) After delivery the ammonia and amino-acid nitrogen remain increased, whereas the peptid nitrogen sinks sharply to normal. (3) In the urine of eclamptics shortly after delivery the excretion of peptid nitrogen remains greatly increased and falls only gradually. (4) Alimentary levulosuria and increased excretion of peptid nitrogen were parallel generally during pregnancy. (5) The ammonia increase is probably due to liver impairment. In creased peptid nitrogen is possibly the result of increased excretion of aromatic and hydro-aromatic acids paired with glycoll.

The Urinary Findings in Cancer.—E. SALKOWSKI (*Berl. klin. Woeh.*, 1910, xlvii, 2297) referred, in a previous communication, to an unusual division of the nitrogenous constituents of the urine in patients suffering with cancer. Kojo, working in Salkowski's laboratory, has devised simpler methods of examination, and with these a few urines have been examined. The method (details of which are to appear in a subsequent paper) employs the following manipulations. The phosphates and sulphates are first removed from the urine by precipitation with alkaline barium chloride solution (2 volumes of baryta water and 1 volume of 10 per cent. barium chloride). The filtrate obtained from 100 c.c. of urine, after accurate neutralization with acetic acid, is precipitated with subacetate of lead; the precipitate is collected quantitatively, washed thoroughly, and its nitrogen content is determined (collodial nitrogen). The percentage of N in the precipitate, taking the total N as 100 per cent., is calculated. The average of the urines of ten healthy individuals was 1.22 per cent. of the total N; in ten cancer cases, 3.03 per cent. The report is only preliminary. It remains to be determined whether such increase is characteristic of cancer alone.

New Methods of Studying the Pulse.—CHRISTEN (*Ztschr. f. klin. Med.*, 1910, lxxi, 390) has perfected a new apparatus which he designates the "energometer" (to be had from the firm of Hausmann, A. G., St. Gallen, Switzerland). By means of it he is able to determine (1) the pressure which suffices to overcome the pulse wave; (2) the energy expended in the cuff to counteract this pressure; (3) the pressure at which the maximal volume of blood meets the cuff; (4) the value of this maximal blood volume; (5) the pressure at which the energy expended in the cuff becomes maximal; and (6) the volume of this maximal energy. Five of these characteristics or measurements (2 to 6) are new. All may be determined with ease. In the text of his article, Christen explains the meaning of each of the factors mentioned and describes the methods of calculation.

Observations on Adhesive and Exudative Pericarditis.—WENCKEBACH (*Ztschr. f. klin. Med.*, 1910, lxxi, 402) publishes observations (1) on the therapy of exudative pericarditis (by the production of pneumopericardium), (2) on pulsus paradoxus, and (3) on the diagnosis of adhesive pericarditis. Under the third heading Wenckebach discusses (a) general circulatory disturbances; (b) hepatic swelling; (c) the systolic retraction of the apex; (d) the pulsus paradoxus, which he shows has a special form in this disease (tracings); (e) the paradoxical behavior of the neck veins on respiration; (f) diastolic collapse of the neck veins; and (g) the abnormality of the respiratory mechanism. The last consists in a fixation of the anterior chest wall due to the adhesions which prevent a forward elevation during inspiration. Wenckebach considers this sign extremely important, and has found it present in all cases which have come under his notice. The anterior chest wall cannot expand in the precordial region with breathing; in fact, it may be slightly retracted during inspiration. In exudative pericarditis, on the other hand, he has found the respiratory movements free. The diagnostic meaning of this sign Wenckebach sums up in these words: "In the presence of this disturbance of the respiratory movements adhesive pericarditis exists in all probability; with free inspiratory elevation of the anterior chest wall adhesive pericarditis is excluded."

SURGERY.

UNDER THE CHARGE OF

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A Case of a Diaphragmatic Hernia in an Adult.—RINGROSE (*Brit. Med. Jour.*, November 26, 1910) says that many cases of congenital diaphragmatic hernia have been collected, but the instances of the

subjects having lived to adult life are extremely rare; and he reports a case occurring in a woman, aged twenty-six years, who had been a school-teacher before marriage and had passed examination by the medical examiner. In November, 1909, she became pregnant, and later said that she had never felt better in her life than in the early months of pregnancy. On May 31, 1910, she complained of feeling sick, and had "dragging" pains in the abdomen and back. At 3 P.M. she vomited. On June 1, when first seen by Ringrose, her face was flushed, the respiration 44, and temperature 100.4°C. The heart apex beat was in the fifth space, a little internal to the nipple line. The first and second sounds were normal. The percussion note over the left side of the thorax was dull up to the second rib; above that it was hyper-resonant. On the left side at the back there was dulness on percussion, weak breathing, and diminished vocal fremitus up to the angle of the scapula. The patient was constantly eructating about a half ounce of clear yellowish fluid. The abdomen was occupied by the pregnant uterus of about seven months. On June 2 the condition continued poor, and aspiration was decided upon, but the child was born about 6 P.M., without labor pains or warning. Two days later the patient became cyanosed and the pulse very weak. She continued to vomit, and died on the following day. At autopsy it was found that the fundus of the enormously distended stomach was situated in the thorax as high as the second rib, there being an hour-glass constriction where the stomach passed through the diaphragm. The large omentum had passed partially through the hernia into the thorax. About a quarter of the small intestine was also in the thorax, and together with the fundus of the stomach and omentum had compressed the lung against the vertebral bodies. The hernial orifice admitted the whole hand, and there was no evidence of any tear or laceration; in fact, the condition suggested a long duration if not a congenital deficiency of the diaphragm. On reducing the stomach and intestines into the abdomen, the condition at once recurred, being suggestive that this migration into the thorax had been of some considerable standing.

Spinal Anesthesia, with Special Reference to the Addition of Adrenalin Preparations to the Anesthetic.—ZUR VERTH (*Deut. Ztschr. f. Chir.*, 1910, cvii, 367) says that spinal anesthesia should be carried no higher than the operation requires. When induced according to this principle, for operations up to the height of the pelvic cavity, it shows no blood pressure fall and is, therefore, without danger. For an estimation of the value of lumbar spinal anesthesia, it is necessary to differentiate between that form which is artificially extended and that in which the anesthetic is distinctly circumscribed. In the latter, complications practically never arise, so that it may be called a completely harmless procedure. The higher the anesthetic reaches, the greater the percentage of complications. Whether the greater extent of the anesthetic area alone or the adrenalin itself causes the frequency of complications by high anesthesia is not decided. We must strive to find an anesthetic substance which in a high-reaching spinal anesthesia will not influence the blood pressure. Until then it is advisable to keep up the blood pressure by heart stimulants, when high spinal anesthesia is employed.

Postnarcotic Paresis of the Stomach.—PAYER (*Mitt. a. d. Grenz. d. Med. u. Chir.*, 1910, xxii, 411) says that in almost all patients, immediately after the passing of the narcotic sleep, one can establish a considerable atony of the stomach. Not rarely the lower border of the stomach reaches to the umbilicus, sometimes one or two fingers' breadth lower. The degree of gastric paresis varies very much; only rarely is it not demonstrable. At all events it is independent of the age of the patient. It also has no noteworthy relationship to enteroptosis. These gastric pareses are, in general, of a very benign character. In the great majority of cases they recover in from twelve to twenty-four hours. The postnarcotic vomiting bears a direct relation to the gastric paresis, since in all cases in which the vomiting lasts longer the enlargement of the stomach is demonstrable during this period. The flow of gastric juice is a symptom associated with the paresis; because of the most exact diet in not a few cases, a rather abundant vomiting was observed. The critical period of the gastric paresis is from the third to the fifth day when ordinary solid nourishment is begun. When no new symptoms appear it is observed that with the taking of food the borders of the stomach are contracted in a striking manner, and the more so the longer after the narcosis the taking of food is delayed. Children show the greatest contraction in an especially striking manner. Errors in diet influence the paresis very unfavorably. Here also the children are most affected. In them up to the eighth day after the narcosis one occasionally sees a marked distention of the stomach. At times drainage of the peritoneal cavity has a bad influence on the stomach. Enteroptosis and chronic dilatation of the stomach are of special importance only so far as the enlargement of the stomach from paresis is much more distinct. Payer does not use any other method of emptying the dilated stomach than to allow the contents to have an opportunity to escape by placing the patient in a suitable position. In the use of position Payer sees the best and only method of effective treatment. The following changes in posture are recommended: Elevation of the pelvis, lying on the abdomen, on the right side, on the left side, knee-elbow position, knee-elbow changing with lying on the abdomen, extreme knee-elbow position, with simultaneous taxis from the rectum or vagina or in the hypogastrium. Not only does this method improve the condition of the patient, but it paves the way for permanent cure. The best prophylaxis consists in giving attention to the condition of the stomach before and after narcosis, in placing the patient during postnarcotic vomiting immediately in the right-sided position, so that no blockage of the flow of gastric juice can be produced, and in providing a most exact regulation of the diet in the first four or five days.

The Diagnosis of Wounds of the Spleen.—LEVY (*Zentrbl. f. Chir.*, 1910, xxxvii, 1577) calls attention to the frequency with which successful operations have been done of late for wounds of the spleen, and says that little attention is being paid to a very valuable symptom for diagnosis. He reports a case of wound of the spleen in a healthy young man, the physician who saw the case soon after the accident making a diagnosis of a simple contusion of the abdomen. The family physician who was called in a little later found, in addition to pain in

the whole abdomen, severe pain in the left shoulder. Because of the increasing shock, the distention of the abdomen, the marked right-sided rigidity, and the severe tenderness in the region of the spleen, a wound of the spleen was diagnosticated. Levy first saw the patient in the evening, and agreed with the diagnosis. He was particularly impressed with the fact that the patient's chief complaint was of the pain in the shoulder. Immediate laparotomy established a wounded spleen. This organ, which was exposed with difficulty because adherent to the diaphragm, showed two large rents, one near the hilum and the other on the convex surface. Splenectomy was performed, and three weeks later the patient was discharged, cured. Pain referred to the right shoulder is very characteristic of abscess of the liver. The pain in the left shoulder from wounds of the spleen, as on the right side, is explained by the association between the phrenic and fourth cervical nerves. Other symptoms are, frequently, sufficiently distinct to establish the diagnosis of wound of the spleen, but where they are not prominent the pain in the left shoulder may be of much value. Opinions differ as to whether the treatment should consist of tamponing the splenic wound, suture of it, or extirpation of the spleen. Most surgeons, however, will extirpate the spleen if the rent is deep. A tampon usually does not secure against hemorrhage, and most surgeons hesitate to employ the suture method. Levy's patient, before he was hardly well after the splenectomy, was severely burned in an explosion, but recovered from this accident, showing that his general resistance was not much impaired by the removal of the spleen. Since in severe burns there is destruction of many red blood corpuscles, which are usually restored by the spleen, it would appear that the bone marrow acts in a manner sufficiently compensatory for the removed spleen.

A Method of Producing Experimentally Acute Hemorrhagic Pancreatitis.—SEIDEL (*Zentrbl. f. Chir.*, 1910, xxxvii, 1601) divides the pylorus transversely, closes the gastric and duodenal ends, and re-establishes the communication between the stomach and intestines by a gastroduodenostomy. Ten to fourteen days later the abdomen is again opened and above the gastro-enterostomy, but below the entrance of the pancreatic duct, the duodenum is constricted by a broad band, tightly enough to prevent the passage of intestinal contents but not tight enough to produce necrosis. This prevents the escape of bile and the secretion of the upper part of the duodenum, while the gastro-intestinal passage is free. Death followed regularly in twenty-four hours. The pancreas becomes the seat of a very severe hemorrhagic necrosis. In a few instances fat necrosis was present. The isolated portion of the duodenum was strongly dilated, and suggested that the rapid death was probably due to the form of ileus which was present. The question arose in Seidel's mind as to whether a violent peritonitis could not have developed from infection passing through the wall of the intestine, which might also have led to bacterial inflammation and hemorrhage of the pancreas. Several control experiments were carried out in which the original occlusion of the duodenum and gastroduodenostomy were performed. In two the pancreas, atrophied from oil injections, was extirpated. One dog died in eighteen days. The isolated portion of duodenum was changed into a thick-walled

tumor, the lumen of which was only 3 mm. wide and communicated with the lower part of the duodenum through the constricted portion. The second dog died in four days. He had a diffuse peritonitis from a perforation of the intestine at the site of the ligature of the duodenum. In another control experiment the pancreas was preserved, but its main duct was divided between two ligatures. In other respects, in this experiment, the procedure was the same as in the main experiment. In another animal, the duodenum was ligated above the entrance of the pancreatic duct. These two animals died in three and four days after the ligation of the duodenum which was always done at a second operation. There was peritonitis from perforation at the site of the ligature, but the pancreas was completely intact. These control experiments showed that it is possible to produce an acute hemorrhagic pancreatitis only by a back flow from the intestine to the pancreas, and that other factors—ileus from obstruction of the intestine and infection of the pancreas—are to be excluded.

Blockage of the Extremities as a Simple Method of Saving Blood and Chloroform in Operations on Other Parts of the Body.—HANS (*Zentrbl. f. Chir.*, 1910, xxxvii, 1579) has been for about six months employing the method of contracting the circulation during general anesthesia by applying tourniquets to the extremities, and he believes that as a consequence there is less bleeding in operations on the head, neck, and trunk, and even on a non-obstructed part of an extremity. The method may be applied for hemorrhages occurring during childbirth and internal hemorrhages. Less chloroform or ether is necessary. In an emergency, or for the purpose of more quickly arousing the patient, one can obtain a very energetic autotransfusion from the blood held back in the extremities. The method was employed by the ancients for the control of severe hemorrhages of the lungs, and is still regarded as of value for the same purpose. Hans applies the small rubber tube near the axilla and groin under slight tension before beginning the administration of the anesthetic. He withholds the chloroform until there is a bluish red congestion of the extremities. The veins are almost completely obstructed by the tourniquet and the arteries only partially, the back pressure completing the blockage in them. The blood in the extremities is then free of chloroform and the brain obtains much less of the anesthetic, since it is accessible only to that in the blood of the trunk and head. If the narcosis should become too deep, the chloroform free blood of the extremities may be liberated and the depressed heart thus revived.

The Fate of Buried Silver Wire Netting for the Closure of Hernial Orifices.—RIEM (*Archiv f. klin Chir.*, 1910, xciii, 973) made a study of the literature and of the patients in whom wire netting was implanted by Körte. In 4 the netting was later removed on account of a persistent serous or suppurative discharge. Of the remaining 16, Riem has investigated 10, and has received a written report from another. The x-rays have been employed to determine whether the netting was intact and had remained in place or not. By palpation only a thickening can be determined which is largely made up of cic-

tricial tissue. Eight years have elapsed since the operations were performed. According to the results of his studies it can be said that the hope that the netting remains in its original form and site of fixation and that it closes permanently the weak place in the abdominal wall has not been fulfilled. The silver wire will be gradually eroded by the acid-containing body juices and will break. It lies embedded in thick, firm cicatricial tissue, which prevents, in many cases, danger from free wire ends. It does not appear, however, that trouble cannot arise from this cause. The x-rays teach us that the netting, under some circumstances, migrates or sinks, so that the large vessels (external iliac and deep epigastric arteries) may be penetrated by the projecting end of the wire. Wounds of other organs, as of the bladder or intestines, are possible. The removal of a netting broken and embedded in a cicatricial tissue is not easy. In one case its removal required an extensive operation, which destroyed the cicatricial closure of the hernial orifice. It follows that wire netting is not an ideal substance for closing the hernial openings and that it should be employed only in exceptional cases, in which Trendelenburg's implantation with bone plate is not feasible, for instance in old decrepit persons with atrophic bones.

Partial and Circular Closure of Intestinal Fistulæ with Skin.—RAKITZKY (*Archiv f. klin. Chir.*, 1910, xciii, 1021), after experiments on dogs, devised an operation for the closure of certain intestinal fistulæ of the abdominal wall with protruding margins. The operation was performed by Professor Radjan as follows: An oval incision about 10 cm. long and 8 cm. wide was made around two intestinal fistulæ, one representing the open end of the ascending colon, the other that of the ileum, and both being in the median line near the umbilicus. They had been left after a resection of the intervening portion of the intestine and were a few inches apart. The incision was about three inches from the fistulæ on all sides. A flap of skin and subcutaneous tissue was dissected centrally about two and one-half centimeters, turned inward and the edges united together in the median line by sutures, which resembled Lembert sutures. This made a closed skin-lined canal with a diameter of about 3 cm., an anterior wall 10 cm. long, and a posterior wall of about 2.5 cm. This canal served as a communication between the two intestinal fistulæ, and thus continued the previously interrupted fecal current. Then both recti muscles were exposed by a longitudinal incision in the anterior layer of the sheath of each, and the inner edges of both brought together by sutures over the turned flap of skin. The anterior layers of the sheaths of the recti were then united, and then the skin. A drainage tube was left in at the lower angle of the wound. At the upper and lower angles small fecal fistulæ formed, but at the end of two months they closed spontaneously. The boy is now well, a half year after the operation. Rokitzky found that in a similar manner such an operation had been previously employed in 6 cases in Biondi's clinic in Siena, in all with an ideal result. He had had no knowledge of these cases before he performed the operation on his case.

THERAPEUTICS.

UNDER THE CHARGE OF

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Report of 375 Cases Treated with "606."—SIESKIND (*Münch. med. Woch.*, 1910, lvii, 2027) reports 375 cases of all stages of syphilis treated with Ehrlich's remedy. His article contains many valuable details, and should be consulted in the original. No deaths occurred in this series of cases. The following indications are given for the use of "606": (1) Cases of malignant and early ulcerating syphilis, especially those refractory to mercurial treatment. (2) Syphilis in any stage when mercury is not well borne. (3) Cases of recurrence after repeated mercurial treatment. (4) Cases of syphilis in the early incubation period. When possible, the chancre should be excised or destroyed by the Hollander hot-air method. Injections of small quantities of the remedy into the local lesion also aid in the treatment. (5) Syphilis associated with tuberculosis, since mercurial treatment has often a bad effect upon tuberculosis. (6) Cases of visceral syphilis. (7) Decrepit patients, even though they have no organic disease. (8) Cases of latent syphilis when the Wassermann reaction persists. (9) Parasyphilitic affections in various stages. Sieskind also gives the following contraindications: (1) Grave non-syphilitic optic nerve diseases. (2) Severe organic disease of heart or bloodvessels. (3) Severe pulmonary disease, except tuberculosis. (4) Severe kidney disease, not of syphilitic origin. (5) Advanced degenerative disease of the central nervous system. (6) Cases of angina or febrile diseases. The injection is postponed until the fever disappears in such cases.

Magnesium Poisoning.—Boos (*Jour. Amer. Med. Assoc.*, 1910, lv, 2038) reports 10 cases of poisoning after the administration of magnesium sulphate. In 7 of the cases there was no cathartic effect from the magnesium sulphate, but, on the other hand, the salt seemed to cause a paralysis of the bowel. This paralysis was so marked in 2 cases that laparotomies were performed. A marked diminution of the urine also occurred, amounting in some almost to anuria. Vomiting occurred in about half the cases, and in only 1 case was there active purging. This patient took the salt in several pints of beer, and possibly this death may be attributed to the violent purging. Convulsions and motor paralysis were observed in 2 cases. A striking effect was the depression of respirations that occurred in 6 of the cases. Boos draws the following conclusions: (1) Magnesium sulphate in bulk or in concentrated solution is absorbed, in part at least, from the gastrointestinal tract into the blood. (2) If a sufficient amount of the salt is absorbed, at a given time poisoning will result; of the 10 cases reported, 6 resulted fatally. The symptoms and autopsy findings in these cases agree very well with those obtained in animals after the intravenous

application of magnesium sulphate. (3) On account of the slowness of its excretion from the system, magnesium sulphate, given repeatedly in concentrated solution, may produce poisoning by cumulation. (4) In normal condition of the bowel, magnesium sulphate, in proper dilution, is a valuable cathartic. (5) It is not wise to give magnesium sulphate indiscriminately in cases of so-called acute intestinal obstruction, because when peristalsis is much diminished or absent, and in cases of mechanical obstruction of the bowel, even dilute solutions will be absorbed, with consequent danger of poisoning. (6) In cases of suspected magnesium poisoning, large quantities of normal salt solution should be given intravenously. Dilute solutions of lime salts given hypodermically may also be of benefit. (7) The subcutaneous use of magnesium salts to produce catharsis, as proposed by Wade, is not only absolutely irrational, but dangerous.

The Use of Typhoid Vaccines in Typhoid Fever.—ANDERS (*Jour. Amer. Med. Assoc.*, 1910, lv, 2023) discusses the results obtained by different clinical observers with the use of vaccines in the treatment of typhoid fever. These results are extremely variable, some writers reporting favorably and others finding either no especially striking effects or entirely negative ones. Anders reports 8 cases treated with vaccines, with no striking results. Small doses of vaccine were employed, namely, initial doses of 25,000,000 and subsequent ones of 50,000,000 each. These injections were repeated at intervals of seventy-two hours. The author believes that phagocytosis probably plays an important role in the cure of typhoid fever, and therefore a vaccine should stimulate an increased leukocyte count. Anders found that the doses of vaccine he employed did not appreciably increase the leukocyte count. He warns against the use of the vaccine method in severe cases when the system is already overwhelmed with the typhoid bacillus and its toxins. He also states that an anti-endotoxin would constitute the ideal method of treating typhoid fever. Anders concludes by saying that vaccine therapy in the treatment of typhoid fever should receive a more extended trial than hitherto, more particularly in the earlier stages of mild types of the disease, before being rejected. Finally, in the present state of our knowledge, the value of vaccines for the following purposes must be conceded: (1) As a means of prophylaxis; (2) in suitable cases when continued during convalescence to prevent relapses; (3) to combat local infections with the typhoid bacillus, as, for example, bone suppurations which arise in the period of convalescence; and (4) for the removal of the typhoid bacilli from the feces and urine in the case of typhoid-carriers.

Treatment of Typhoid Fever with Vaccines.—HOLLIS (*Med. Record*, 1910, lxxviii, 622) compares the vaccine treatment of typhoid fever with the older method of treatment by hydrotherapy. Eleven cases were treated by vaccination and the results compared with 21 cases treated under similar conditions with hydrotherapy. The diet in both methods of treatment was of the high caloric variety. No drugs were employed, but strychnine and whiskey were used as stimulants in the severe cases. The bowels were moved with enemata. Those treated by vaccination received no baths other than a daily warm soap and water sponge. No

fever reaction was obtained. No case ended by crisis. Occasionally a slight local erythema or itching was noticed at the point of injection, which cleared up without treatment. The agglutinins were markedly stimulated by the vaccines. Complete agglutination was observed in dilutions as high as 1 to 500 or 1 to 1000, while cases without vaccines showed incomplete agglutination in 1 to 80 dilutions. No effect was noted upon the temperature or length of the disease. Hemorrhage was seen with equal frequency in both classes of cases, though not so severe in those vaccinated. Relapses were noted with more frequency in the vaccinated cases—30 per cent. as compared to 10 per cent. No death occurred in the vaccinated cases, although there were four in the other series: one from hemorrhage, one from perforation, one from toxemia, and one from pulmonary thrombosis with necrosis of the whole left upper lobe of the lung. Headache, gastro-intestinal symptoms, and toxemia were far less frequent in the cases treated by vaccination than in those treated by hydrotherapy, and convalescence also seemed to be more rapid. Hollis usually gave from 10,000,000 to 50,000,000 dead bacilli by subcutaneous injection. The injections were given in the region of the buttocks, every second or third day. He says that the number of cases is too small to draw any definite conclusions, although the results obtained in individual cases were often so striking that they seemed to indicate almost a specific action.

The Clinical Use of Strophanthus.—HATCHER and BAILEY (*Jour. Amer. Med. Assoc.*, 1910, lv, 1697) state that the clinical use of digitalis has proved one of the greatest problems of medicine, and despite the advances made in our knowledge of the pharmacology of this group, the problem has advanced only, not solved, and there are few practitioners who can invariably distinguish the toxic action of digitalis from the symptoms of cardiac disease. The choice of the member of the digitalis group which is to be used in a given case, whether it shall be digitalis itself in the form of the tincture or the infusion, or one of the active principles, such as digitalin, digitalinum verum or digitoxin, or whether it shall be strophanthus, strophanthin, or ouabain, must be considered mainly as a question of administration, and not with the view to securing any essentially different action, until we know more of the differences following equivalent doses. At the present time we have two pure digitalis principles available—crystalline ouabain and crystalline digitoxin. The ouabain may be used in sterile solution, but the digitoxin is insoluble in water. The preparation ordinarily known as strophanthin is methyl ouabain. The average therapeutic dose of crystalline ouabain, of crystalline strophanthin, so-called, by intravenous injection is about 0.5 mg., the equivalent of 1.5 mg. of digitoxin or 4 c.c. of a good tincture of digitalis. It is obvious, therefore, that the dose of strophanthin used is much too high, or that of the other digitalis bodies is too low, for it must be remembered that the dose by the vein is far less than that by the mouth. They say that the tincture and the infusion of digitalis represent the leaf fully, and that the idea must be abandoned that the action of one is different from that of the other. Hatcher and Bailey's conclusions are as follows: The intravenous injection of crystalline ouabain affords the most exact dosage possible in digitalis therapy, and the most rapid effect. It is quite

possible that any Galenical preparation of digitalis or strophanthus will be found available for intravenous or intramuscular injection, but the activity should be determined in terms of crystalline ouabain on the mammalian heart. The cardiac action of any digitalis body is elicited promptly after the intravenous injection. The oral administration of the digitalis bodies will continue to be preferred for the general treatment of cardiac disease, and in such cases the tincture or infusion of digitalis deserves the preference, because they are more readily absorbed than the preparations of strophanthus. We are in urgent need of more exact clinical studies of all of the digitalis bodies, particularly with regard to their relative effects on the centres and on the vessels, and we are in equally urgent need of further pharmacological investigations of the rate of absorption and excretion of these several bodies, with an elucidation of the phenomenon of cumulation.

PEDIATRICS.

UNDER THE CHARGE OF

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Urobilinuria in Scarlet Fever.—WILHELM HILDEBRANDT (*Münch. med. Woch.*, 1910, lvii, 2512) has investigated the efficiency of the liver in scarlet fever and found that in the greater number of cases there was a pathological urobilinuria. This urobilinuria followed the temperature curve fairly constantly, increasing with high temperature and gradually diminishing as the temperature came down. In one of his cases he was able to determine a high degree of urobilinuria some time before the typical rash appeared and just preceding the initial high rise of temperature. During convalescence an increased urobilinuria is, as a rule, no longer found. A very strong urobilinuria in the beginning of a case in which the diagnosis lies between scarlet fever, measles, diphtheria, or lacunar angina is a symptom which strongly indicates scarlet fever. Urobilinuria is extremely rare in diphtheria, and when present in the other conditions, is of a lesser degree. The production of the urobilinuria in scarlet fever Hildebrandt believes to be an acute scarlatinal parenchymatous hepatitis, although a beginning hemolysis is a possible element in its production. The demonstration of urobilinuria in a case, and thereby of a parenchymatous hepatitis, is important from the standpoint of treatment. Severe cases which show a urobilinuria extending into the period of convalescence should be kept in bed and put on appropriate diet. The more severe forms may go on to acute yellow atrophy of the liver. The demonstration of the presence of urobilinuria is the safest and surest test of the presence of parenchymatous hepatitis. Pediatricists should find out the amount of urobilin in the urine in all cases of scarlet fever, for it may easily be the case that a parenchymatous

hepatitis is the beginning of a subsequent cirrhosis of the liver, just as an acute scarlatinal nephritis is often the beginning of a future chronic nephritis.

Thyroid Extract in Chorea.—PERCY A. RODEN (*Lancet*, 1910, clxxix, 1276) reports a case of chorea in a girl, aged ten years, which is interesting from a therapeutic viewpoint. The condition was acute and the arms and legs were especially affected. The heart was not involved. The child was treated over quite a long period of time on each of the following remedies: arsenic, potassium iodide with potassium bromide, salicylates, and quinine. Absolutely no improvement resulted from the use of any of these drugs. Brine baths were then employed in a hospital, and the patient's condition was apparently relieved by them. In a month's time the chorea again appeared with wasting. Cod-liver oil with the bromides and iodide of potassium having no effect, the brine baths were again tried and again apparently relieved the condition. After several months the chorea reappeared. At this time it was noticed that the two sisters of the patient had goitre, but were in perfect health. On examination the patient showed no trace of goitre. On this suspicion of thyroid insufficiency, teaspoonful doses of fluid extract of thyroid gland were administered twice a day, with surprisingly good results. The child was able to return to school in the second week. The thyroid was taken twice a day for the first month and once a day for the second month. After nine months had elapsed there had been no recurrence of the trouble

Calomel as a Diuretic.—FELIX V. SZONTAGH (*Archiv f. Kinderheilk.*, 1910, lv, 121), while agreeing on the diuretic action of calomel, takes exception to the statements of various pediatric authors that calomel is a fitting and excellent diuretic in nephritis. He claimed that calomel is contraindicated in true nephritis. Aside from any general diuretic action, calomel, as an end result, acts as a strong irritant to the kidneys and in large doses may set up a desquamative nephritis. In this he agrees with Leube who also warns against the use of calomel in renal dropsy in children. Szontagh tends to the belief that dropsy, up to a certain point, prevents uremia, the poisonous matters being held in solution and temporarily withdrawn from the circulation; and that it is a questionable practice to induce a large and free diuresis by calomel in such a case, thus causing a reabsorption of the poisons in large quantities, which tends to the development of uremia. In these cases of renal dropsy, with threatening uremia, the possibility of cardiac insufficiency is of greater importance. An increase of diuresis by calomel would in this case do the heart no good. He claims that calomel should not be exhibited for its diuretic or purgative action in renal dropsy or in postscarlatinal nephritis. It is his belief and experience that the domain of calomel as a diuretic lies entirely in cardiac dropsy. He comments on the absence of this fact in pediatric publications and text-books where calomel in this connection is spoken of as a "two-edged sword" and a dangerous drug. He cites several cases of cardiac dropsy, as an illustration of his general experience, in which digitalis, strophanthus, and caffeine had no appreciable effect on the dropsy, but when calomel was administered for its diuretic effect, it brought up

the urine output invariably from 200 c.c. to 2000 c.c. and even as high as 4800 c.c. By using calomel in this way he has prolonged life at least a year in hopeless cases. He has had no bad results in the way of mercurialization in his cases, and he claims that calomel is the most efficient remedy for reducing severe cardiac dropsy in a short time, without danger of mercurialization.

Rare Occurrences in the Rheumatism of Childhood.—F. J. POYNTON (*Brit. Med. Jour.*, 1911, ii, 5) urges the importance of accepting the view that rheumatism in childhood is an infection. Early recognition of the symptoms is the first step in successful treatment, and this is made possible only through a thorough medical inspection of school children. His observations on the rarer forms of rheumatism in childhood are based on a series of 600 cases. Rashes in rheumatism are usually urticarial and erythematous, and in 600 cases, Poynton found them present at the beginning of the disease in 40 cases. At times the rash simulates scarlet fever and exhibits a rapid, branny desquamation. Chorea, joint complications, or endocarditis frequently follow rheumatism. He mentions the tendency to purpura in acute rheumatism, and cites a number of cases in point. Pemphigus and herpes are found in rare instances, and a combination of several of these forms has been observed. Erythema nodosum, while not proved to be an effect of rheumatism, is probably closely allied to it. Tachycardia is an occasional occurrence in rheumatism, and occasionally persists for a long time. Prominence of tachycardia with irregularity is often found where the heart muscle has suffered more than the valves. He has never seen an enlargement of the thyroid gland in the rheumatism of childhood. Mastitis occurs occasionally.

Further Reports on the Influence of "606" on Congenital Syphilis through Mother's Milk.—J. PEISER (*Berl. klin. Woch.*, 1911, xlviii, 13) refers to four recorded cases of remarkable disappearance of the lesions of congenital syphilis in infants when the nursing mothers were treated by "606" injection. These cases are reported by Tæge, Duhot, Debrovits, and Scholtz. Of these, Scholtz was the only one who reported finding traces of arsenic in the mother's milk, the quantity being less than $\frac{1}{10}$ mg., forty-eight hours after the injection. From these records it would seem not only right but obligatory to try "606" on nursing mothers with syphilitic children. But Peiser reports two cases treated by Dr. Ritter in Berlin which tend to modify the apparent obligation. One child, eight days old, showed lesions of congenital syphilis on its body and had visceral lues at birth. The mother showed no syphilitic signs. The Wassermann reaction was positive in both mother and child. The general condition of the child was poor and the prognosis bad. In the second case the infant developed a syphilitic eruption shortly after birth and had "snuffles," but its general condition and the prognosis were good. The Wassermann reaction was positive in mother and child. In both infants, after their mothers were injected with "606," the lesions and the syphilitic conditions were somewhat improved, but shortly became worse and both children died. The autopsies showed affections of the lungs, liver, kidneys, and bones typical of congenital syphilis. The internal organs of the first child showed no spirochetes.

Many spirochetes were found in the suprarenal glands of the second infant. No traces of arsenic could be found in the mother's milk in either case. These two cases show that this method of treatment in congenitally syphilitic infants cannot be relied upon absolutely. In this connection Rosenthal reports a case of congenital syphilis in an infant in which injection of "606" in the nursing mother was followed by an increase in the syphilitic condition of the child. Recourse was then had to mercurial treatment, which gave satisfactory results.

OBSTETRICS.

UNDER THE CHARGE OF

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The Nature of Eclampsia.—MURRAY (*Jour. Obst. and Gyn., British Empire*, October, 1910) describes experiments made to determine the natural hemolytic power of foetal serum on animal corpuscles; the presence or absence of iso-agglutinin in normal foetal serum; and the presence or absence of hemolysin in the foetal serum of diseased pregnancies. A length of umbilical cord was tied and cut off at delivery, wrapped in cotton and placed in an incubator, and examined never later than twelve hours. Part of the contained blood was separated by centrifuge after clotting, and only tubes were used in which clear serum formed. Washed red cells were prepared by dropping blood directly into citrated saline, washing three times in saline, and neutralizing in a 5 per cent. suspension. Equal parts of serum and suspension were mixed in small sterile tubes with a diameter of 1 c.e., incubated for two hours at 37° C., and placed in an ice chest. The normal hemolytic power of animals was investigated for rabbits and guinea-pigs. The hemolytic power of normal adult serum on rabbits' washed red cells varies greatly. Different human sera act with varying rates on the same rabbits' corpuscles, and corpuscles of a series of rabbits are hemolyzed at different rates by the same human serum. In various intoxications these differences are still more marked, diabetes having a very high co-efficient, and uremia a low one. The same variation in power was shown in foetal serum. On the average, the rate of hemolysis was very much slower; each of the fifteen sera tested hemolyzed 5 per cent. suspensions of the red cells of rabbits and guinea-pigs. The times taken to perform this had no apparent relation to the times for the corresponding maternal sera. The conclusion is that of other observers, that the natural hemolytic power of maternal sera is greatly in excess of that of the foetus. The opportunity was taken of comparing the hemolytic power of 10 maternal sera on rabbits' washed corpuscles with 10 male and 10 non-pregnant female sera. No variation from the normal limits was found. The effort to obtain agglutination and hemolysis was invariably negative. In 10 cases

of normal pregnancy 40 combinations of the serum of one foetus with the corpuscles of another, were tried. In one case of albuminuria with much oedema, foetal serum less normal corpuscles, was tried without result. In one moderately severe case of eclampsia, with recovery of the mother, and death of the foetus, a like negative result was obtained. A negative result regarding the presence of foetal agglutinins or lysins, or maternal or other homologous corpuscles, was obtained in normal pregnancies, and also in stillbirths. In catarrhal jaundice, albuminuria, and eclampsia, a like negative result was obtained. These experiments were confirmed by observations upon guinea-pigs immunized to foetal blood by intraperitoneal injections of pooled blood from umbilical cords. No agglutination was seen in any. It would appear from these experiments that foetal serum is wanting in iso-agglutinins, and that it does not develop iso-hemolysins in diseased pregnancies. It cannot, therefore, cause the hemotoxic lesions found in pregnancy. In 3 cases of eclampsia whose postmortem findings are reported, the blood serum did not hemolyze normal red cells. The results from the foetus proving absolutely negative, an investigation of hemolytic bodies from the placenta was next undertaken. Nine placentæ were investigated, 3 full term normal, 2 premature, and 4 eclamptic. The lipid substance was extracted from a convenient quantity of the whole placenta minced. Small pieces were preserved for microscopic examination. The eclamptic placenta yielded a lipid material capable of extraction by ether. These lipid substances were markedly more hemolytic than in the normal placenta. Investigations were then undertaken to determine whether these lipoids were capable of acting as antigens. A very pure lecithin was employed, and on adding varying quantities of 1 per cent. emulsion, a very marked hema-agglutinative power was present, which the addition of lecithin absolutely prevented. There was then no evidence found of any prolecidithide element in these lipoids, as they did not differ from the ordinary lipoids of degenerating tissues. They are, however, present in larger quantities in eclamptic placenta and are hemolytically more active than in normal pregnancy. This may be comparable to the increase of lipoids which occurs in the liver after hemotoxic injections. The placenta is as rich in enzymes as the liver, and may suffer in a similar manner. The condition known as anaphylaxis consists of serious and fatal attacks with convulsions, at certain times, and with certain quantities of complex albuminous substances, not poisonous when administered in the same quantity as a solitary dose. This phenomenon has been studied by inoculating guinea-pigs with horse serum, but various other proteids of alien origin, such as egg albumin, milk, and sterilized bacterial products, produce the same result with great certainty. Peptone is not so effective, and lucin and tyrosin are ineffective. The first dose takes nine or ten days to sensitize the animal. At a later period toxic symptoms develop, usually rapidly followed even by death, and within a few minutes by convulsions. Under other conditions, cough, nasal irritability, ascending paralysis, and possibly convulsions, may develop, followed by recovery. To produce these phenomena the proteid must be alien, and the refractory period of nine or ten days must be present, when the serum of the sensitized animal will, on inoculation into another

of the same species, passively sensitize it, so that the animal is at once ready to receive the second autotoxic inoculation. Where death occurs slowly in these cases the pathological findings closely resemble those of eclampsia. In experimenting upon this matter, Murray concluded that it was the autolytic rather than the purely placental element which produced the anaphylaxis. The evidence, however, was not satisfactory that eclampsia is anaphylactic in nature. The clinical picture is different, and the experiments narrated did not point to a positive conclusion. In the 3 cases with postmortem examination, the characteristic lesions of eclampsia were found in the liver, the spleen, and in the retroperitoneal glands.

Appendicitis Twenty-four Hours After Labor.—CHILL (*Jour. Obst. and Gyn., British Empire*, October, 1910) reports the case of a primipara delivered under chloroform by forceps. Twenty-four hours after labor the mother was seized with violent pains in the epigastric region, spasmodic in character, accompanied by gaseous cructations. The temperature and pulse were normal, the uterus was contracted and free from pain or tenderness. There was a history of similar paroxysms of pain at intervals for several years previous to marriage. In spite of opium and turpentine enemas, the pain extended to the right iliac fossa, and tenderness with vomiting and constipation, were present. On opening the abdomen the appendix was found thickened and perforated at its base, and was removed. The patient died on the following morning.

Three Cases of Pregnancy Following Salpingectomy.—POLAK (*Amer. Jour. Obst.*, October, 10, 1910) reports the case of a patient who had borne a child, but since parturition had suffered from pain, profuse discharge, and frequent and burning urination. A laceration of the pelvic floor, a bilateral tear of the cervix with erosion, salpingitis, a cystic and prolapsed left ovary, and a tender appendix, were found. The patient was operated upon and made an uneventful recovery. Some months afterward she returned, complaining of pain and a burning sensation on the right side, and the right Fallopian tube was found tender on examination. After a few local treatments, she disappeared, and returned three years later. In the interval she had borne two children, and then complained of pain on both sides, backache, and increased menstrual flow. Examination showed relaxation of the outlet, a small anteфлекed, tender uterus, and an enlarged and tender right tube. She again entered the hospital, when the uterus was curetted, the cervix amputated, the pelvic floor restored, and the right tube removed. She made a good recovery. Four months later she returned in a pregnant condition and subsequently passed through the pregnancy and had an uncomplicated labor. In the second case the patient was operated upon for dermoid of the right ovary, which was removed with the tube, and the uterine end of the tube was excised into the cornu. This line of incision was closed with a continuous catgut suture, care being taken to close the uterine muscle and peritoneum over the mouth of the tube. She was afterward again admitted to the hospital with ruptured interstitial pregnancy at the right cornu. The cornu was excised, and the patient made a good recovery. It

is interesting to observe that the fecundated ovum had migrated into the interstitial portion of the right tube, which had previously been excised, and the muscle and peritoneum closed over its abdominal opening. The third case was one which had been operated upon for double tubal disease, and the tubes probably ligated and ablated but not excised. She was afterward admitted with symptoms of ectopic gestation and abdominal hemorrhage. An interstitial pregnancy of eight weeks' development was found in the stump of the right tube which was attached to the ovary of that side by adhesions. The remains of the left tube projected from the left uterine cornu. The ruptured tissue of the right cornu was excised and the tissues accurately closed.

Purulent Catarrh of the Tube After the Production of Artificial Abortion.—AMERSBACH (*Monatss. f. Geburts. und Gynäk.*, 1910, xxxii, Heft 4) reports a series of cases from Aschoff's institute in Freiburg in which specimens of Fallopian tubes removed after cases of abortion, were examined. It was found that after a normal pregnancy in labor there was no inflammatory reaction in the Fallopian tubes; but that after dilatation of the cervix with laminary tents, although careful asepsis had been employed in a large majority of cases, there was an inflammation of the tube which had gone on to purulent salpingitis and lymphangitis. This pathological observation is increased evidence of the difficulty of conducting vaginal operations in an absolutely aseptic manner.

The Treatment of Postpartum Hemorrhage.—HOFSTATTER (*Monatss. f. Geburts. und Gynäk.*, 1910, xxxii, Heft 4) reports from von Rosthorn's clinic, 422 cases of postpartum hemorrhage in 32,180 cases of labor. Among these were 205 cases of hemorrhage complicating spontaneous birth, polyhydramnios, and twin pregnancy, and surgical interference practised during labor, there were 253 cases of hemorrhage from adherent or retained placenta or membranes, expression of the placenta, premature separation, and placenta prævia; bleeding occurred from cervical lacerations in 36 cases; while in 34 the cause was hemophylia, nephritis, secondary hemorrhage, cardiac lesions, eclampsia, and myoma of the uterus. In all, there were 13 fatal cases of hemorrhage, none of which could be said to be purely atonic bleeding. In the 32,180 births, 13 deaths from hemorrhage gives a mortality of 0.04, a result comparing favorably and approximating closely that of other clinics. Four of these 13 patients died of premature separation of the placenta; 6 from placenta prævia; 1 from a tear of the cervix; 1 from nephritis; and 1 from bleeding through a retained portion of the placenta. The cervical laceration was produced by Bossi's dilator; the patient with nephritis died the day after delivery with acute anemia. In the 13 fetal deaths the tampon was employed in 11 cases; in 5 cases where the tampon failed to check hemorrhage, total extirpation of the uterus was practised through the vagina, but too late. In discussing methods of treatment, the use of the tampon, bimanual compression of the uterus, the immediate application of the suture to tears in the genital tract, the use of pituitrin and adrenalin, have all given good results. Vaginal douches after the delivery of the placenta are

dangerous through the possibility of infection. Intrauterine injections of the solution of gelatin are condemned. In 2 cases, Momburg's application of the elastic bandage was tried with apparently good results. In 1 case hemorrhage ceased, the patient could be put in bed and stimulants given, and pituitrin injected intravenously. After several hours the gauze tampons in the uterus and vagina became saturated with blood and were removed, and lacerations in the cervix and deep lacerations of the vagina were closed. There was secondary relaxation of the uterus, which was afterward controlled. In a second case, the application of Momburg's bandage for half an hour seemed effectual in checking the bleeding. The patient's general condition and respiration improved markedly after its application. It is thought that its use, however, is dangerous in lesions of the kidney and liver because of the stasis caused in these organs.

GYNECOLOGY.

UNDER THE CHARGE OF

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The Sensibility of the Internal Genital Organs.—During the course of an operation for prolapsus under local anesthesia, BROSE (*Zentral. f. Gyn.*, 1910, xxxiv, 1523) had the opportunity to test the sensibility of normal pelvic organs. Separation of the bladder from the cervix was painless, although not infiltrated with the anesthetic. The tissue immediately beneath the uterovesical fold of peritoneum was extremely sensitive and necessitated application of the anesthetic before it could be incised. Nausea was produced by the introduction of the fingers into the peritoneal cavity. When traction was made upon the uterus, the patient complained of considerable pain; following displacement into the vagina the pain ceased. Pinching, squeezing, and the application of heat and cold to the tubes, ovaries, and uterus failed to produce discomfort. Division of the tubes, suture of the cornua, and ligation of the mesosalpinx were painless. These observations are in accord with those of Lenander, who claims that all organs which are supplied by the sympathetic or vagus after giving off the recurrent nerve are not sensitive to pain, pressure, heat, or cold; pain resulting from disease of these organs is due to stimulation of the spinal nerves through participation of the parietal peritoneum in the diseased process. Müller and Goldscheider deny this assertion, and claim that while the visceral nerves are not sensitive under normal conditions, disease renders them so. Bröse thinks that the diagnosis of ovarian neuralgia should never be made; the symptom complex thus described in text-books has nothing to do with the ovaries, but is merely a manifestation of hysteria.

Hematoma of the Ovary.—HEDLEY (*Jour. Obstet. and Gyn. Brit. Emp.*, 1910, xviii, 21) bases his study upon 18 cases of hematoma of the ovary, observed in St. Thomas' Hospital during the past ten years. He claims that this is a comparatively common affection of the ovary and one whose importance as a pathological entity deserves greater consideration on the part of clinicians than it has thus far received. Hematoma is a condition in which the ovary is enlarged and contains fluid resembling old altered blood of a tarry or oily consistence. In the great majority of cases it is found in the child-bearing period of life; the affection is associated with a marked diminution in fertility. Menstrual disturbances, especially menorrhagia and dysmenorrhœa, are frequently present. With but two exceptions, pain was the most prominent symptom; the onset may be sudden and severe, with subsequent cessations and exacerbations at varying intervals; there may be only dysmenorrhœa or a continuous dull aching pain. The physical signs vary with the size of the hematoma and the stage of the inflammatory reaction; fixation of the mass was a striking feature in all but 2 cases examined. The temperature is usually normal or only slightly elevated. Hedley describes the gross and microscopic appearances and points out the fact that while the ovary is always surrounded by dense adhesions, there is usually no evidence of gross tubal disease. The formation of a hematoma can be ascribed to the rupture of several Graafian follicles into one another instead of on to the surface of the ovary separately. The etiology is still obscure; while pelvic congestion from one cause or another has been considered an important factor, it cannot be held responsible in all cases. It is probable that the accumulation of blood is due to failure of the mature follicles to rupture when hemorrhage takes place into them. Important from its bearing on the etiology and pathology is the observation that a bacteriological examination of 2 cases revealed a pure culture of staphylococcus albus. The diagnosis is seldom made prior to operation. Treatment consists in removal of the diseased ovary; when bilateral, an attempt may be made to leave a piece of normal ovarian tissue by dissecting away the lining of the hematoma.

Pure Cultures of Blastomycetes from Malignant Tumors.—After reviewing his previous work on the subject and summarizing the conclusions of various other observers, LEOPOLD (*Archiv f. Gyn.*, 1910, xcii, 31) details his technique and describes the appearance of the blastomycetes. By examining the most recently formed tissue from malignant, non-ulcerating tumors, he was able to demonstrate the blastomycetes in 50 out of 64 cases; pure cultures were obtained in 37 out of 50 cases. In the last 22 cases the tissue was subjected to fermentation, and in every instance were blastomycetes demonstrable. Following inoculation of three rats, intra-abdominal tumors developed, which killed the animals; from these tumors blastomycetes were again obtained in pure culture.

Some of the Newer Conservative Treatments for Pelvic Infection.—Of the various conservative measures employed in pelvic inflammation, GILLMORE (*Surg., Gyn., and Obstet.*, 1910, xi, 574) looks with greatest favor upon bacterial vaccinations, although thus far an insufficient number of cases has been reported to warrant definite conclusions.

While the remedy offers no promise to cure the infection primarily, considerable evidence is afforded to show that in those cases of low resistance vaccinations are of undoubted value. Following Schindler's observations, he advises the use of atropine in gonorrhœal infection, which is continued during the acute stage to arrest contractions of the uterus and tubes and thus prevent an extension of the disease upward. While tamponade, douches, and massage have a distinct place in the treatment of inflammatory conditions, the cases must be carefully selected for such treatment, bearing in mind not only the medical but also the personal aspect of the patient. In the presence of a pelvic exudate with normal temperature, pulse and leukocyte count, Gillmore advises the application of dry heat to the abdomen by means of a modified Gellhorn apparatus. He concludes by mentioning the new electrical instruments devised by Gschwend, which give promise of excellent results.

Hematocolpos.—PRONAI (*Frauenarzt*, 1910, xxv, 482) draws the following conclusions from a study of 19 cases: In the majority of cases of gynatresia, incision and circular suture will suffice; the opening must be large to guard against subsequent contraction. Even when a diagnosis of hematosalpinx has been made, a laparotomy is not indicated when the tumor is not large; such a procedure, under aseptic precautions, is associated with no danger. Since the discharge of the blood takes place slowly and offers an excellent culture medium for the growth of organisms, the hematocolpos should be thoroughly evacuated at the time of operation.

Torsion of the Fallopian Tube as a Factor in the Etiology of Hematosalpinx Apart from Ectopic Pregnancy.—After reporting a case of hematosalpinx with torsion of the tube, McILROY (*Jour. Obstet. and Gyn. Brit. Emp.*, 1910, xviii, 368) discusses, first, the etiology of hematosalpinx without torsion. While the great majority of cases are due to ectopic gestation, the condition may be associated with uterine pregnancy and atresia of the genital canal caused by malformations or tumors; other factors are tubal menstruation, inflammatory conditions and tumors of the tubes and disorders of circulation. With regard to torsion of the tube, the author concludes from this study of the literature that there is no one definite cause for the rotation of the pedicle, but that when torsion does take place, followed by strangulation, there is an effusion of blood into the tissues and cavities of the organ or tumor involved. In the majority of cases of hematosalpinx apart from ectopic pregnancy the cause is to be looked for in a torsion of the tube, as a rule at the uterine end. Predisposing causes, such as congestive conditions, weakness of the vessel walls, and tumors of the tubes, are to be taken into account. The exciting cause of the rotation may be found in the mobility of the tube in conjunction with increased intra-abdominal pressure. Peristaltic action of the lower bowel has undoubtedly some influence in favoring axial rotation. That torsion should occur in a perfectly healthy tube must be of rare occurrence, although histological examination of series of tubes in the various stages of fetal development shows that flexions of these organs are frequently present. The

direction of the torsion and the number of twists are of little importance clinically; the degree of strangulation is what should be looked for on examination of the tube.

The Best Method of Exposing the Interior of the Bladder in Suprapubic Operations.—In a well illustrated article, KELLY (*Surg., Gyn., and Obstet.*, 1911, xii, 30) describes a new method which he has devised for exposing the interior of the bladder. After the bladder has been irrigated, a mushroom catheter large enough to fill the urethra is introduced. With the patient in the Trendelenburg position, a transverse incision is made through the skin and fat about one inch above the symphysis pubis concave toward the umbilicus and about six inches long. The upper skin and fat flap is dissected free and the fascia covering the recti and oblique muscles is divided transversely, avoiding the underlying muscular tissues. By blunt dissection the recti are separated from their fascial attachments, permitting easy retraction of the muscles. An inflating rubber bulb is now attached to the mushroom catheter and the bladder is filled with air to bring it up into the wound. Two guy sutures are inserted into the bladder, which is opened transversely as far as is necessary to expose the lesion presented. The transverse incision is decidedly the best one for the bladder, as it gives the widest possible opening, parallel to the opening in the fascia of the abdominal wall, and perfectly avoids all risk of injuring the peritoneum; the incision also lies parallel to, and not across the course of, the vesical vessels. The opening in the bladder is closed and the abdominal wound sutured with or without drainage as the case demands.

The Permanent Results of Abdominal Total Extirpation in Carcinoma of the Uterus.—In 1901 Glockner published the results of 260 vaginal operations for carcinoma of the uterus performed in the Leipsic clinic. AULHORN (*Archiv f. Gyn.*, 1910, xcii, 231) bases his study upon 377 cases in which the abdominal operation of Wertheim has been employed since 1902, thus affording an excellent opportunity for comparison of the two methods from the same clinic, from the same material and the same operator—Zweifel. The average operability in the abdominal cases was 65.7 per cent., rising from 50 per cent. in 1902 to 80 per cent. in 1908; at the time of the vaginal operation the operability was 26.6 per cent. The primary mortality of the abdominal operations was 13.1 per cent.; in the vaginal, 6 per cent. In estimating the percentage of permanent cures only those cases were chosen which had gone five years or more without a recurrence; in addition all cases of corpus carcinoma were excluded. Estimating the results according to Winter's formula, 51 per cent. were permanently cured with 25 per cent. of absolute cures; with the vaginal operation 34 per cent. were permanently cured, and absolute cure resulted in 9.7 per cent. The value of glandular extirpation is shown by the fact that no recurrence took place in five patients from whom carcinomatous glands were removed. In two women there was recurrence after five years. In those cases requiring resection of the bladder, rectum, or ureters, on account of carcinomatous infiltration, recurrence invariably took place. The bladder or the ureters were injured in

4.5 per cent. of the cases, while postoperative necrosis occurred in 3.6 per cent. of the cases. Only by decreasing the primary mortality and increasing the operability can the results of operation for carcinoma of the uterus be improved. With regard to the former, Aullhorn advocates Zweifel's extraperitoneal extirpation and Bumm's drainage of the peritoneal cavity through the vagina in addition to the radical vaginal operation of Schauta and Staude. According to the experience of the Leipsic clinic, an increase of operability through the selection of more advanced cases and hence more radical operations is hopeless. While thus far education of the public has proved of but little value, still further efforts must be made along this line, since this is the only means whereby better results can be obtained in operations for carcinoma of the *uterus*.

The Significance of the Lane Kink of the Ileum.—MARTIN (*Surg., Gyn., and Obstet.*, 1911, xii, 34) summarizes his article as follows: The Lane kink of the ileum has its location in the last six inches of the intestine at and before its attachment to the cecum. The pathology occurs at this point of the ileum because of the comparatively fixed condition of this part of the gut due to its short mesentery. The actual cause of the bend in the intestine and the adhesions complicating it and the change in its mesentery are due to traumatism as a result of the prolapsed cecum dragging upon it, or the pulling of the balance of the small intestines upon it, or the grinding of superimposed viscera that are subject to abnormal descent upon it. The pathological anatomy exhibited in the kinks are bending of the ileum in one or more places obstructing its lumen, shortening and thickening of its mesentery, adhesions of the folds of the mesenteries together, adhesions of the arms of the kinked bowel to each other and to other intestines, rolling of the intestine in its own mesentery, and adhesions to it in such a way as to materially lessen its lumen. The causes of the descent of the cecum, the small intestine, and the superimposed viscera, which apparently precipitate the pathological kink, are a congenital defect in the individual in which mature blending of the peritoneal surfaces failed to materialize, and acquired defects which weaken the supports of the abdominal viscera. The symptoms are acute, colicky pains, a dull steady pain due to chronic stasis subject to exaggeration when the intestines are overloaded. The location of the pain being, according to Lane, one inch below and to the right of the umbilicus, occasional attacks of acute and subacute obstruction relieved by recumbent position and dieting, anorexia, indigestion with a tendency to large gas formation, and general toxemia due to intestinal absorption. The treatment, laparotomy, separating of adhesions, straightening the intestine, replacement of the organs causing the kink, rearranging viscera with omentum employed as a protector and bolster while the patient is in the Trendelenburg position, application of strong supports, adhesive plaster corset, reinforced by pressure pads on the lower abdomen held tight by adhesive straps, constant wearing of abdominal supporters applied in the Trendelenburg position, supplemented each day by abdominal massage administered while in the Trendelenburg position.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF
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Paralysis of the Right Vocal Band in a Case of Myotonia Atrophica.—FOX (*Jour. Laryng., Rhin., and Otol.*, December, 1909) reports a case of myotonia atrophica in which the patient's method of rising from the recumbent position resembled that met with in pseudohypertrophic paralysis. The right vocal cord was fixed midway between the cadaveric and phonatory positions. There was no evidence of any lesion of the vago-accessory nerve, either centrally or peripherally. The case was shown in order to elicit opinions as to whether the laryngeal lesion was a part of the general condition or otherwise. The trend of the discussion was to consider the condition as myopathic.

Suture of Recurrent Laryngeal Nerve.—HORSLEY (*Jour. Amer. Med. Assoc.*, January 15, 1910) reports an apparently unique case of successful suture of the recurrent laryngeal nerve. Three months after an injury by bullet wound, all the muscles supplied by the left recurrent laryngeal were found completely paralyzed. An incision disclosed the injured nerve in the groove between the œsophagus and trachea. The diseased portion was excised, with the exception of a small filament consisting of the posterior part of the nerve sheath. The ends of the nerve were brought together with a single suture of No. 0 chromic catgut in a fine curved needle. The wound healed by first intention, and the patient left the hospital nine days thereafter without improvement in voice or in breathing at that time. Nevertheless improvement was gradually going on, and a report from a laryngologist about two months after operation showed improvement in the muscles, and a second report, fifteen months after the operation, stated that the laryngeal muscles supplied by the left recurrent laryngeal nerve had fully recovered.

Acute Nephritis Following Acute Tonsillitis.—LOEB (*Jour. Amer. Med. Assoc.*, November 12, 1910), as a result of an experience with acute nephritis, finds that it is a frequent sequel of tonsillitis overlooked by the great majority of practitioners, the nephritis being of the hemorrhagic type, and the symptoms ordinarily not manifested until some time after the inception of the disease.

Emphysema Immediately Following Tonsillectomy.—PARISH (*Laryng.*, November, 1910) reports seeing a case to which he was called because of alarming symptoms having developed while the patient was being carried from the operating room. The operator told him that there had been nothing unusual in the operation except possibly more bleed-

ing than customary, but that there had been a small buttonhole made in the lower portion of the posterior palatine fold in the dissection. When Parish reached the ease, breathing was rapid and shallow, pulse about 128 and thready, face livid and lips cyanosed, the head and neck extended far back and quite rigid, and the skin cold and moist. The entire neck of the patient was puffed out so that the line of the jaws was entirely obliterated, both cheeks and right eyelid swollen, and the crackling of emphysema easily detected over this entire area, and as far down as the last rib anteriorly. Under forcible opening of the jaws, the use of tongue forceps, and bending the head and neck forward the general condition became rapidly better, and the patient underwent an uneventful recovery.

Stenosis of the Pharynx as a Result of Operation for Adenoids.—COURTADE (*Annales des mal. de l'oreille, du lar., du nez, et du pharynx*, August, 1910) reports a case of a child, aged seven years, who had been operated upon at four years of age for adenoid vegetations without accident, but without any amelioration in the difficulty of respiration. A year afterward a second operation was performed under anesthesia. After returning home the patient passed a great deal of blood by vomit and by stool. In a third operation enlarged tonsils were removed without special incident. The mother stated that the child had never breathed freely by the nose, and continually kept the mouth open. Courtade found an incomplete velopharyngeal adhesion consecutive, in all probability, to the second intervention. The pharyngeal orifice behind the uvula was too small to permit the passage of an adenoid curette.

Acute Thyroiditis with Œdema of the Glottis Following Exposure to Epizootia of Horses.—LEWIS and O'NEILL (*Jour. Amer. Med. Assoc.*, November 12, 1910) report this case: A hostler, aged fifty-six years, while engaged in his usual work, suddenly fell to the ground in a choking fit from œdema of the larynx attended with rapid and great enlargement of the thyroid gland. Under morphine, ice-bag about the neck, and adrenalin spray whenever the dyspnoea became excessive, dyspnoea and hoarseness, the most marked symptoms, disappeared within three days, and on the fourth day the patient was able to leave the hospital and go back to work.

Eyestrain a Cause of Exophthalmic Goitre.—GOULD and DURAND (*Jour. Amer. Med. Assoc.*, December 17, 1910) contend that they have had a considerable number of cases, of which one is detailed, showing causal relation of eyestrain and Graves' disease. Mydriasis is suggested as a method of testing whether the early symptoms of exophthalmic goitre are due to eyestrain.

A Binocular Stereoscopic Laryngeal Telescope.—HEGENER (*Jour. Lar., Rhinol., and Otol.*, November, 1910) has constructed a telescope for stereoscopic binocular inspection of the larynx, rhinopharynx, and auditory meatus, as an adjunct to ordinary measures of examination in special cases.

DERMATOLOGY.

UNDER THE CHARGE OF

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Treatment of Eczema.—W. SCHALTZ (*Deut. med. Woch.*, October 14, 1909) deals with the principles governing the treatment and the etiology and the anatomy of the disease. Toxic causes are sometimes important factors which must be eliminated before a complete cure is to be hoped for. External treatment alone in these cases is insufficient to effect cure. The use of water locally in moist eczema he regards as injurious, not so much from the contact of the water as that the natural oil is thereby removed from the epidermis.

Pellagra.—F. M. SANDWICH, of London (*Jour. Amer. Med. Assoc.*, November 13, 1909, p. 1659), who has had a large experience with this disease, states that there are certain general axioms which hold good in Italy and Egypt, and doubtless will be found to apply to the United States. Thus, in districts where no maize (*zea mays*) is cultivated or habitually eaten, pellagra does not exist. There are many countries where maize has been cultivated for many years and yet pellagra has not appeared. Well-to-do people in pellagra districts, living on varied diet and consuming maize as an occasional and not as the staple cereal, usually escape pellagra. It is not good maize or good maize flour which produces pellagra; the disease requires for its production the habitual use of damaged maize in some form.

Pellagra, Ancient and Modern.—HOWARD D. KING (*Jour. Amer. Med. Assoc.*, November 6, 1909) gives the history of this interesting disease, with its notable cutaneous lesions, which has of late received so much attention in this country, and shows that cases and epidemics have been from time to time recorded, and not confined to States with warm climates. During the period of the rebellion in this country the records do not contain specific instances of cases bearing even a resemblance to pellagra, which is noteworthy considering the lack of hygiene and proper food of the troops in the field. In the South, corn was one of the chief (if not absolutely the only one) articles of diet, and yet, if the disease existed to a large extent, no mention was made of the fact. The disease of late has been reported as existing mostly in sporadic form in many of the States.

Lichen Planus.—D. W. MONTGOMERY and H. E. ALDERSON (*Jour. Amer. Med. Assoc.*, October 30, 1909) state that they believe lichen planus to be a distinct affection, and also to be a constitutional disease

with manifestations on the skin and mucous membranes. A striking case illustrating the acute generalized form is narrated, in which lesions bore a resemblance to syphilis, especially inasmuch as the papules and tubercles were remarkably firm. There was also a resemblance to lepra, but no bacilli were found. There was severe itching. The gastrointestinal tract was very sluggish. There were marked and varied constitutional symptoms, and the course of the disease was slow and prolonged. The authors believe that a toxin is at the bottom of such cases, acting much in the same way as the ferments which produce urticaria, and that the nervous symptoms generally admitted by dermatologists as being pronounced in most cases may be explained in this way rather than by considering the disease of nervous origin.

Barley Itch.—W. K. WILLS (*Brit. Jour. of Dermatology*, August, 1909) reports cases in which the skin was affected with a profuse rose-colored papular eruption of an urticarial nature, contracted by men engaged in unloading a cargo of barley from Northwest Africa. Out of eighteen porters engaged in the work, fifteen were affected. On examination with a lens, some of the papules were seen to contain a tiny black dot, which proved to be minute lancee-pointed hairs with a fractured proximal end and an air-containing central medulla. No fungus nor animal was detected either in the barley or the dust. Microscopic examination of specimens of cowhage (*Mucuna pruriens*) showed a resemblance to the dust from the barley in question. Simple local treatment proved all sufficient to effect a cure.

The Employment of Kromayer's Quartz Lamp in Eczema.—RAVE (*Archiv f. Dermat. u. Syphilis*, 1910, ci, Heft 1), who successfully treated with the quartz lamp 12 cases of eczema of various types, which had resisted all other methods of treatment, believes that this lamp deserves to be employed in obstinate eczemas more frequently than it is. He believes it should be tried in obstinate, recurring vesicular, eczemas which have failed to respond to other forms of treatment, including the x-rays; in pustular eczemas of the scalp and beard to prevent relapses; and in chronic eczemas with infiltration, of the psoriasiform type, for the removal of the infiltration. In certain cases characterized by infiltration of the connective tissue accompanied by acute exacerbations, a combination of Röntgen and quartz lamp irradiation is useful.

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THE
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ORIGINAL ARTICLES.

THE THERAPEUTICS OF DIGITALIS AND ITS ALLIES.¹

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IN 1775, William Withering, a Birmingham physician, had his attention drawn to a family receipt for the cure of dropsy long kept secret by an old woman in Shropshire; he found it composed of some twenty herbs, of which he concluded that foxglove was the essential one. After trying it in his practice for some months he "ventured to assert" that this herb "merited more attention than modern practice bestowed on it." These were the days of deliberate observation in medicine however, and it was not until after ten years careful use of it in his practice that he gave his results to the world,² although he had induced many of his friends to use it in the meantime. In his "account of the foxglove," he recognizes its action on the heart,³ but is chiefly interested in its diuretic effects, and does not associate the latter with the cardiac changes. Withering's work directed immediate attention to the new remedy; I find it given an assured place by Barton, of Philadelphia, in 1798. But its true sphere of action was obscured by its being recommended as a cure for phthisis, although its dis-

¹ An address delivered before the Harvey Society of New York, January 14, 1911.

² An account of the foxglove, and some of its medical uses with practical remarks on dropsy and other diseases. By William Withering, M.D., Birmingham, 1785. This work bears the appropriate motto *nonumque prematur in annum*, and ought to receive attention as an example of the careful observation of the time; it may be added that it may help to dispel some of the apprehensions of the "eumulative" and other dangerous effects of digitalis which are too prevalent.

³ "It has a power over the motion of the heart to a degree yet unobserved in any other medicine and this power may be converted to salutary ends," p. 192.

coverer denied it any usefulness in this disease from the beginning. Later it slowly resumed its position as the cardiac remedy par excellence, but curiously enough not as a cardiac tonic, but as a depressant. Sixty years after its introduction into regular medicine Pereira, the great authority of his day, recommended it chiefly "to reduce the force and velocity of the circulation" as in aneurysm and hemorrhage of internal organs. In his time the new method of experimental investigation of the effects of drugs on animals was in its infancy, but it was soon afterward applied to digitalis by Traube, Schmiedeberg, and others, and the action of digitalis and its allies on the organism was ascertained with certainty in many respects, although it still requires further elucidation. The knowledge of its therapeutic use has also advanced since Pereira's time, and few would venture to recommend digitalis in hemorrhage and still fewer in aneurysm at the present time. But this advance in the therapeutic applications has scarcely kept pace with that of the experimental investigation. Too often the diagnosis of cardiac abnormality, the discovery of a murmur, is regarded as an immediate indication for digitalis, so that in the narrower sphere of the circulatory diseases, digitalis suffers today from the same over-appreciation as was its fate a hundred years ago, when to some minds it appeared to be a panacea for all internal disorders. The advance in the diagnosis of heart disease in recent years, however, gives hope that the sphere of action of digitalis may be more circumscribed, and that we may soon reach a point where instead of "trying digitalis" in every case of heart disease we may be able to define the symptom complex which indicates its exhibition as accurately as that for quinine.

It has long been my feeling that the study of experimental pharmacology should be merely the preliminary to investigation in therapeutics, and I very gladly accepted the invitation of my friend Dr. James Mackenzie to associate myself with him in his clinical researches on the effects of drugs on the circulation. Our final object is to differentiate the types of heart disease in which digitalis is useful, and I may say at once that some progress has been made in this direction. Incidentally we have carefully noted the effect of digitalis and its allies on the human heart and circulation with the view that one or the other might be preferable in certain conditions. We are still far from achieving our goal, but a certain amount of information has been acquired, and when your president did me the honor of asking me to address you, I thought that nothing I could offer would be more appropriate to a society that honors the great name of Harvey than a contribution to the therapeutics of the great remedy in diseases of the circulation.

In the experimental laboratory it is found that digitalis affects the heart in several different directions. In the first place, it was recognized early by Traube that the heart is slowed by stimula-

tion of the inhibitory centre in the medulla. Since his time inhibition of the heart has been shown to depress not only the rate, but also the strength of contraction, the conductivity and the tone of the muscle, so that these must be taken into consideration in any account of the changes induced by the drug. On the other hand, digitalis acting directly on the heart muscle increases the strength of contraction, the tone and the excitability. Its direct effects on conductivity have not been accurately determined. The effects of digitalis on the mammalian heart are, therefore, compounded of two influences which in most instances oppose each other. The rhythm is slowed by the inhibition and accelerated by the muscular action, but in moderate quantities in animals the former prevails and the rhythm is slower. The strength of contraction and the tone are reduced by the inhibitory stimulation and increased by the direct action on the heart, and the changes observed are the resultant of these two; in the ventricle the muscular effect prevails and the chamber beats more strongly, and at any rate, in the dilated heart, relaxes less than before the administration. In the auricle, the inhibitory prevails over the muscular factor, and the result is a decrease in the strength of contraction very often, or it may be there is little change to be noted in this chamber from digitalis. In animals the blood pressure rises from contraction of the arterioles which are acted on directly by the glucosides.

In these experiments in animals, the drugs are injected intravenously in order to elicit the effects quickly enough to permit of their being observed within the limits of an experiment of at most three to four hours' duration. In the therapeutic use of digitalis, however, one seldom sees much change from the drug under thirty-six to forty-eight hours. In addition, the dose given experimentally is often very much larger in proportion than that in therapeutic use, and this, together with the rapidity with which it is thrown into the circulation, must cause a much greater concentration in the blood than is induced in therapeutics. Great caution must, therefore, be used in applying the results obtained experimentally in therapeutics, and perhaps this has not been sufficiently appreciated; I cannot cast a stone at any one. But these experimental investigations, at any rate, show that inhibition and muscular action may be elicited in animals by this series, and encourage us to look for these effects in man.

In Dr. Mackenzie's clinic the patients are, of course, examined by his well-known methods, and the course of the disease and the effects of treatment are constantly controlled by graphic tracings in addition to the ordinary clinical notes. Conclusions may, therefore, be drawn with some confidence from a small number of cases. The disorders of the heart were all of such seriousness as to necessitate admission to hospital and detention there, often

for months at a time. The treatment with digitalis was almost always preceded by rest in bed for a week or more in order to eliminate as far as possible the error of attributing to the drug changes really due to the general conditions. The disorders of the heart on which we have made our observations, may be conveniently thrown into two great groups: (1) Those in which the dominant rhythm of the heart continued to originate in the normal point (Keith-Flack node), and (2) those in which the rhythmogenic function was usurped by some other part of the heart, in our cases by the auricle. The effects of digitalis are so different in these two groups that I shall describe them separately.

In the first group digitalis often caused considerable improvement in the general condition, manifested in relief of the dyspnoea or dropsy, or lessened cyanosis, though the benefit was much less obvious than in the second group of cases. This improvement in the general condition was sometimes accompanied by moderate slowing of the pulse which fell from 90 to 110, to 70 to 80 per minute. But this is by no means elicited in every case even when the other symptoms are relieved. Thus, of 18 patients of the first group, only 6 showed any slowing under digitalis, and in one of these it may be questioned whether this was due to the drug. We can safely say that the pulse was slowed by digitalis in only about 30 per cent. of the cases in which the dominant rhythm was of normal origin. In 2 of our 6 cases, the pulse was previously very rapid and it is possible that excessive activity of the rhythmogenic node may favor this effect of digitalis; on the other hand, if this excessive activity arises from fever digitalis often fails to induce slowing. In the other cases in which slowing followed the use of digitalis no feature was observable which distinguished them from those in which no such effect occurred. During the slowing the heart beat continued to bear its ordinary character; in other words, the slowing is due to fewer impulses being emitted by the rhythmogenic area.

The slowing of the heart under digitalis is universally attributed to stimulation of the inhibitory centre in the medulla oblongata, and in fact it bears every resemblance to the effects of such stimulation. Thus the slowing is not uniform, the rhythm varying with the phases of respiration, as it does in normal individuals with marked inhibition. And this respiratory variation may be developed under digitalis in persons in whom it is previously absent or hardly perceptible. Owing to the development of this feature, the intervals between successive pulse beats may show larger variations after digitalis than before, as Wenckebach has recently pointed out, although perhaps his description tends to exaggerate the significance of this feature.

Further evidence that the slowing is inhibitory in origin is offered by the observation that it disappears under doses of atropine which

have no further effect than to prevent the inhibitory impulses reaching the heart. And finally it has been noted that in complete block, digitalis does not slow the ventricle as might be expected if it retarded the heart by direct action on the ventricular muscle, while the auricle continues to be slowed as in the normal heart.

The question arises why digitalis fails in so many instances to slow the heart. We may exclude at once inactivity of the drug because our preparations were assayed pharmacologically and on treating two patients with the same tincture in the same doses, the one may respond by marked slowing, while the other shows no such effect even when the drug is pushed until nausea and vomiting are produced. Either the centre in the medulla is incapable of stimulation in these recalcitrant cases, or it is incapable of holding the heart in check. It is known that the control ordinarily exercised by the inhibitory centre over the heart varies in different individuals and at different ages in the same individual, and evidence is not wanting that the resistance of the heart to the maximal activity of the centre also varies in the same way. In many instances this resistance is great enough to render nugatory the increased activity of the inhibition induced by digitalis; this resistance to inhibition is especially marked in cases of fever, more particularly when the infection is located in the heart muscle itself as in active myocarditis, in which the irritability of the heart must be considered abnormally augmented.

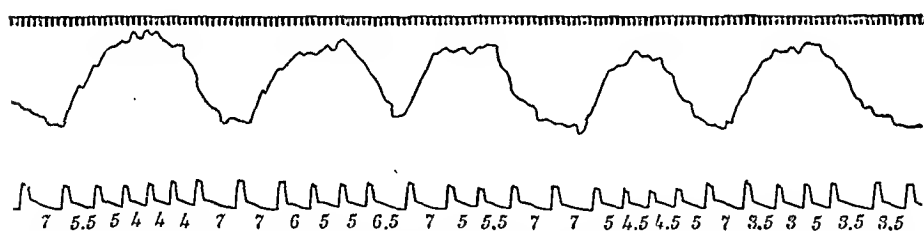


FIG. 1.—Tracing of the respiration (upper) and radial pulse (lower) in patient under digitalis, showing sinus arrhythmia.

When digitalis is pushed further in susceptible cases, the inhibition becomes more marked, and obvious irregularities may appear. One of these, like the general slowing, arises from inhibition of the rhythmogenic area—the sinus irregularity, as it has been called. It often occurs without drugs, and consists in alternate phases of slowing and quickening of the heart corresponding to the inspiration and expiration, and is generally attributed to the inhibitory cardiac centre being involved in the stimulation of the respiratory centre; the stimulus is said to spread to the inhibitory centre. The sinus irregularity of digitalis is sometimes of the same kind, the slowing and quickening corresponding to the movements of respiration fairly closely (Fig. 1). In most cases, however,

this does not hold, the phase of slowing recurring at intervals which are much longer than those of respiration. Here one may suppose that the excited inhibitory centre is aroused by stimuli radiating from some other centre than the respiratory, perhaps from the vaso-motor area. In any case, in this sinus slowing, as in the regular slowing, the contractions of the heart are normal in character, the only departure being a slower generation of impulses by the rhythmogenic centre. I have already mentioned that careful measurements show that in the ordinary slowing from digitalis variations in the rhythm corresponding to the respiration are present. The sinus irregularity is merely an exaggerated form of this induced by larger doses of the drug in susceptible cases.

In other instances in which digitalis is pushed, an irregularity of another kind is developed; the impulses are generated regularly, but fail to reach the ventricle owing to their not being transmitted along the bundle of His. There is, in fact, a partial heart block. The features of this condition have been so fully discussed of late years that it is unnecessary to describe them here. You know how the auricle continues to beat regularly, but every now and then an impulse fails to reach the ventricle and a pulse beat is

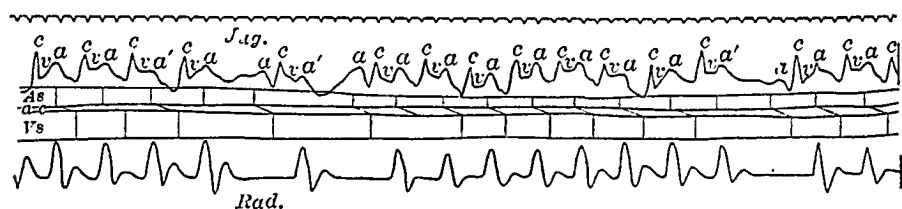


FIG. 2.—Tracing of jugular (upper) and radial pulse (lower) in patient under digitalis, showing occasional failure of the ventricle to contract; a diagram is interposed showing this more clearly. (Mackenzie.)

dropped. This has been noted by a number of observers in the use of digitalis, and has generally been ascribed to the conduction of the bundle having been reduced by the inhibitory stimulation of the drug. It appears to occur especially in cases in which the transmission of impulses is already impaired by disease, as is indicated by the interval between the auricular and ventricular contraction being much prolonged, but it may be induced by digitalis when no impairment of conductivity was detected before; while on the other hand, Mackenzie gives a case in which the conduction was very slow before digitalis, and did not seem to be further depressed by it. This failure of conduction from the auricle to the ventricle under digitalis is universally ascribed to the inhibitory action of the drug, and in fact, has been seen to disappear under atropine, which removes the inhibitory action of the cardiac vagus. This may seem proof positive and I am not prepared to deny that in these cases the inhibition is the potent

factor in the irregularity. At the same time, I am not satisfied that it is the only one; for in animal experiments I have seen repeatedly, in fact it is the general rule at a certain phase of the action, that complete block is elicited, the auricles and ventricles beating independently, and yet this block is independent of the inhibitory action for it occurs after large doses of atropine. I should not be surprised to find that in man also the conductivity of the bundle is impaired by direct action on it and the further lowering of its activity by the inhibitory factor induces the block with which we are all familiar. This irregularity is often accentuated at certain phases of the respiration at which the constant inhibitory influence of the drug is reinforced by the stimulus radiating from the respiratory centre.

These two irregularities from excessive inhibition may occur spontaneously in treatment with digitalis. When they are not present, they may sometimes be elicited by further stimulation of the inhibitory mechanism, direct or reflex. Thus slight pressure on the vagus nerve in the neck is often sufficient to demonstrate this action under digitalis. Latent irregularity may also be discovered in some patients by giving them water to sip. Each time

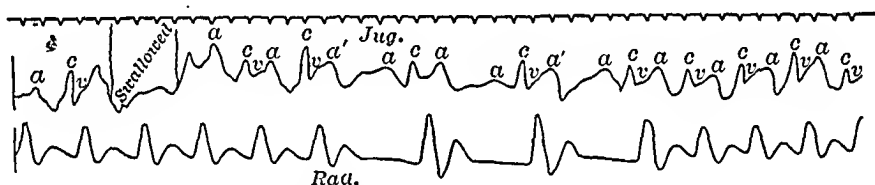


FIG. 3.—Tracing of jugular (upper) and radial pulse (lower) under digitalis in which the rhythm is ordinarily regular, but in which partial block is induced by swallowing. (Mackenzie.)

water is swallowed the pulse is remarkably slowed and either sinus arrhythmia or partial block occurs. Here, I presume, the excitation of the centres governing swallowing radiates to the centre for cardiac inhibition and arouses it to excessive action. As a measure of the recovery of our patients, we often send them up a flight of stairs and then record the pulse rate immediately afterwards. In a number of cases we have noted that the slowing which follows the initial acceleration of the pulse, went on to irregularity, either sinus or block according to the case; in these there was no irregularity except after this slight exertion.

There can, therefore, be little question that the action of digitalis on the inhibitory mechanism which has been investigated in animals, is exerted in a very similar way in a certain proportion of human patients treated with this drug. In moderate degree the inhibition effect slows the pulse, in larger development it may lead to irregularities or, at any rate, favor their development. The sinus

irregularity and the partial block are always preceded and accompanied by slowing. All three features may be developed in the same patient, the sinus irregularity occurring at one time and block at another.⁴ I may add that I elicited and described the phenomena now known as sinus arrhythmia and block by digitalis in the dog many years ago and demonstrated that they were inhibitory in nature. That they occur on stimulation of the vagus in animals is common knowledge.

When we come to look for evidence of the direct action of digitalis on the heart muscle in these cases the position is a much more difficult one, for our present methods of heart examination give very inadequate information of changes in the contractility and tone. I may remark in passing, that here history is repeating itself, for direct proof of the inhibitory action of digitalis was available in experimental investigations on mammals many years before it could be shown to act on the muscle directly. The essential feature of digitalis action in animals in small doses is the stronger beat of the ventricle. In patients, this is difficult to demonstrate. It is true that the apex beat may be considered stronger and the pulse beat larger, but no method of measuring these satisfactorily has yet been devised. And even if this were possible, another difficulty has to be faced; for the heart is often slower, and this in itself would tend to strengthen the contraction of the heart and would increase the stroke of the pulse. So that it is impossible at present to demonstrate directly that the contractility of the heart muscle is increased. Another feature observed in animals experimentally is the lessened relaxation in dilated hearts, and there seemed some hope that this might be demonstrable clinically. But in a number of cases in which we attempted to satisfy ourselves on this point, we could make out no change in the area of cardiac dulness, even when digitalis improved the general condition quite satisfactorily. And the apex beat did not move inward. I do not deny that in some cases these alterations in the physical signs are observable, but in our experience such a change is not by any means always apparent, even when digitalis is exercising its full beneficial effects. In a certain number of cases, however, indirect evidence of the action on the heart muscle may be offered. Thus in a number of patients digitalis failed to reduce the pulse rate or to induce any symptom which could be ascribed to the inhibition; yet in these cases, the embarrassment of the breathing became less, anasarca disappeared and the general condition seemed

⁴ The fact that the slowing, the sinus arrhythmia and block are so frequently seen together while the last two arise from different parts of the heart, suggests that in these patients the abnormality consists in unusual sensitiveness of the inhibitory centre rather than in a low degree of resistance of the heart to inhibition. For there is no reason why both the rhythmogenic centre and the bundle of His should so often show the same variations. And this would imply that the absence of slowing in most cases is due to failure of the inhibitory centre to react to the drug.

improved, and this relief must, therefore, be attributed to the only other factor which we know—the muscular action. Similarly, in some cases in which helleborein was given (in $\frac{1}{2}$ -grain doses t. d. s.), the pulse was not slowed, and no other symptom of inhibition was elicited, but throbbing of the heart was complained of by some patients, and this also seems to indicate change in the muscular contraction independent of the inhibition. I allow that this evidence is very unsatisfactory compared with that given for the inhibitory action, but more adequate proofs can only be expected when more satisfactory methods of measuring the strength of the cardiac contraction are available. At present, we can measure only the rhythm.



FIG. 4.—Tracing of radial pulse under digitalis, showing extrasystole after each normal pulse movement (continuous bigeminy).

Another feature which occurs in animal experiments is the increased excitability of the heart muscle, which makes itself apparent by a tendency to premature contractions or extrasystoles in the ventricle, or auricle and ventricle. These we have very often elicited in patients under full doses of digitalis in the form of more or less frequent extrasystoles (Fig. 4). This augmented irritability is unquestionably the result of the direct muscular action of the drug for, though its occurrence may be favored by slowing of the heart, it often arises in patients who do not present this feature in marked degree. Wenckebach states that extrasystoles may disappear under digitalis medication, but this form of irregularity is so capricious in its appearance that I am not disposed to regard digitalis itself as curative. Another feature which has repeatedly occurred in our cases, although more rarely, is *pulsus alternans*, in which the pulse beats and also the apex beats are alternately large and small without any difference in the interval between them. This form occurs especially after an extrasystole or after a pause of some duration (sinus slowing) and then gradually becomes less marked and disappears. It is met with in untreated cases of heart disease and is generally regarded as evidence of a serious reduction in the contractility. The most satisfactory explanation is that of Wenckebach, who regards the weak beat as the result of the prolonged activity of the preceding strong contraction. It may, in fact, be regarded as a condition in which the recovery of

energy by the heart is retarded, while the dissipation of energy during the contraction is not changed to the same extent or perhaps is unaltered. It may be suggested that digitalis by increasing the contraction power of the heart without a corresponding effect on the restorative function may occasionally tend to favor the development of this abnormality in hearts which are predisposed to it.

Turning to the second group of cases, those in which the node of Keith and Flack has lost its leadership, and the rhythm arises from some other part of the auricle, we find that digitalis has a much more striking effect. In fact it may be questioned whether it would have attained its position as *the* cardiac remedy had it not been for its efficacy in this condition, in which its exhibition is often followed by a truly wonderful improvement. The commonest form of this abnormal rhythm is that known as auricular fibrillation, and there is every reason to infer that a number of Withering's cases were of this description.

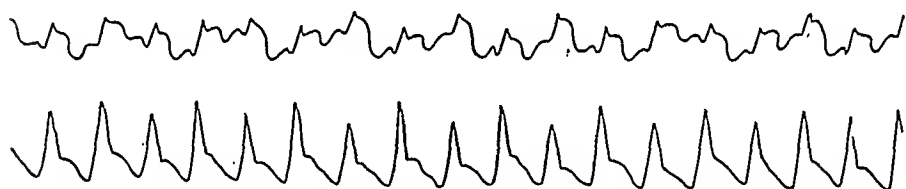


FIG. 5.—Tracing of radial pulse and apex (upper) under digitalis, showing alternation in artery and apex.

In this condition, which has long been known in animals, the auricle is distended and a continual tremulous movement occurs in its fibers, but there is no coördinated contraction, the fibers moving quite independently of each other. Irregular impulses are constantly discharged to the ventricle, which responds with a very rapid and quite irregular rhythm. In man, the condition was first defined by Mackenzie's observations on it, and is characterized by extreme irregularity of the pulse and by the absence of all signs of auricular activity. Its true pathology has only been determined recently. In our cases of this condition, the exhibition of digitalis was generally followed by rapid improvement. It is true that it did not restore the normal rhythm, but the symptoms of heart failure disappeared much more rapidly than in cases of the first group in which the normal rhythm was preserved. And coincidentally with this improvement in the general symptoms the rate of the pulse fell from 120–150, to 60–70 or less.⁵ The

⁵ To ascertain the heart rate with even approximate accuracy in these cases, a record of the pulse must be taken or the heart sounds counted.

pulse remained irregular, but the irregularity was less marked (Fig. 6), and the beats were much stronger; the dyspnoea was relieved and the other symptoms of distress underwent marked improvement. The patient was often able to return to his work if it was not of an exhausting nature.

The most striking objective symptom was the fall in the pulse rate, which offered a marked contrast to that observed in the first group of cases. In these, in which the rhythm arose from the normal position, only about 30 per cent. of the cases reacted to digitalis with slowing, while 11 out of 12 of our cases of fibrillation, or 90 per cent., showed unmistakable slowing. In the twelfth there was fever present and no slowing occurred. The pathology of the condition suggests that this slowing is due to fewer impulses

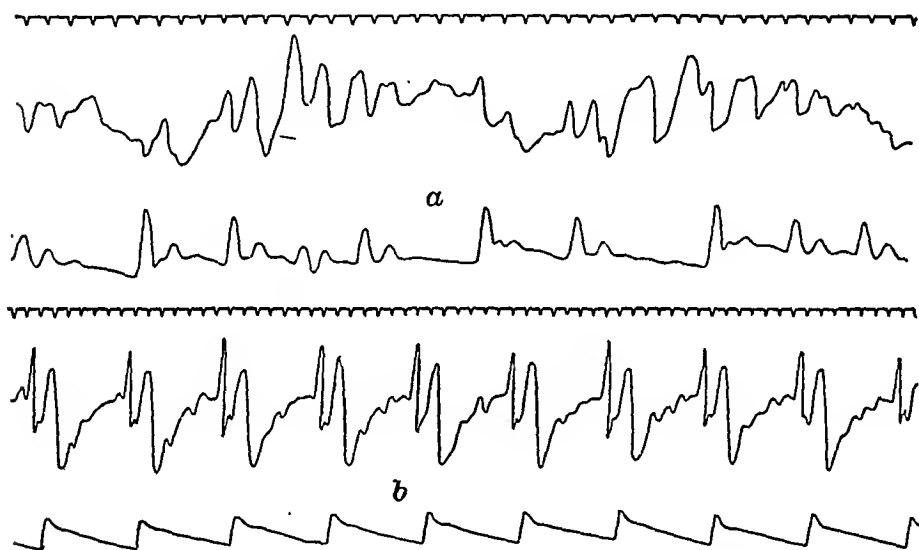


FIG. 6.—Tracing of the jugular (upper) and radial pulse (lower) in a case of fibrillation of the auricle (a) before treatment, (b) after treatment for some weeks with digitalis.

reaching the ventricle from the auricle. The condition of the last chamber is unchanged as far as our means of observation teach us, and there seems no other plausible explanation of the fall in the pulse rate than a diminution in the impulses passing the bundle of His. Moreover, in some rare forms of auricular delirium the pulse though completely irregular is not accelerated, and here there is reason to believe that the impulses from the auricle are partially blocked in their passage to the ventricle; in these cases digitalis does not slow the heart nor cause any marked improvement. Wenckebach has shown that stimulation of the inhibition by pressure on the vagus in the neck in auricular fibrillation induces the same slow pulse as occurs under digitalis, and in a case in which this procedure was ineffective, digitalis also failed to improve the rhythm. One is, therefore, tempted to

attribute the remarkable effects of digitalis in the ordinary forms of auricular fibrillation to its inducing a partial block of His' bundle⁶ and thus relieving the ventricle from the continual bombardment with impulses from the auricle; that is, the digitalis action here would appear to be pure inhibition. And this explanation is supported by our experience in a number of cases in which the distress disappeared as the pulse fell, and when the treatment was given up for a few days the pulse accelerated, and almost step by step with the acceleration of the pulse, the dyspnœa returned.

In several cases the question has been further tested by the injection of atropine in sufficient quantities to put the inhibition out of action. For example, in a case of fibrillation in which the pulse was originally 150-170, but in which it had been reduced by digitalis to 60-70 per minute, $\frac{1}{50}$ -grain atropine sulphate hypodermically accelerated the pulse to about 120. This seems to suggest that the inhibition was a large factor in the effect, though not the only one, for though the pulse was much accelerated by atropine it did not regain its original rate. In another case in which the original rhythm was about 150 per minute, it was reduced to about 50-60 by large doses of digitalis (15 minims four times a day). The patient left the hospital and continued to take digitalis as he felt the need of it, gradually reducing it until after some months he found that his pulse remained slow without the drug, and he only took about a drachm when it began to accelerate, about once a week. Yet on giving atropine at this time the pulse at once rose to 150 per minute, that is, to its original rate. In this case there seems no question that the conduction was reduced permanently by inhibition or, rather, that the inhibition had gained a permanent control over the heart, which was absent before the digitalis was given. Whether this is due to the prolonged inhibition to which the heart had been subjected by digitalis in the hospital, or whether the nutrition of the organ had been altered by some other effect of digitalis, *e. g.*, on the heart muscle, I am unable to say. And the fact that our methods give no sufficient indication of the changes in contraction power must render us careful in the interpretation of the symptoms. But I think I am safe in stating that we have no definite evidence that digitalis exerts any action apart from the inhibition in these cases of auricular fibrillation and that the proved fact of inhibition explains all the features observed.

When digitalis is pushed in auricular fibrillation it often reduces the rate still further to 40-50 per minute and induces "coupled beats;"

⁶ Another possible interpretation may be suggested: In auricular fibrillation inhibition makes the tremor of the auricle finer in character, and perhaps the impulses transmitted to the bundle of His are weaker and thus fewer of them reach the ventricle. Digitalis may, therefore, slow the ventricle by weakening the impulses from the auricle rather than by increasing the difficulties in their passage.

that is, each beat of the ventricle is followed at a very short interval by a second weak contraction and then by a long pause (Fig. 7). The electrocardiograph indicates that the first strong contraction originates in the normal way by an impulse reaching the ventricle from the bundle of His, while the second weak one is a true ventricular extrasystole. In one of our cases in which "coupled beats" were present, atropine accelerated the rhythm of the ventricle by improving the conduction in the bundle and as the rate increased the coupled beats became fewer and finally disappeared. This suggests that the irregularity was at any rate, in part the indirect result of the slow rhythm which allowed the irritability of the ventricle time to develop, and that here the extrasystole resulted indirectly from the inhibition.

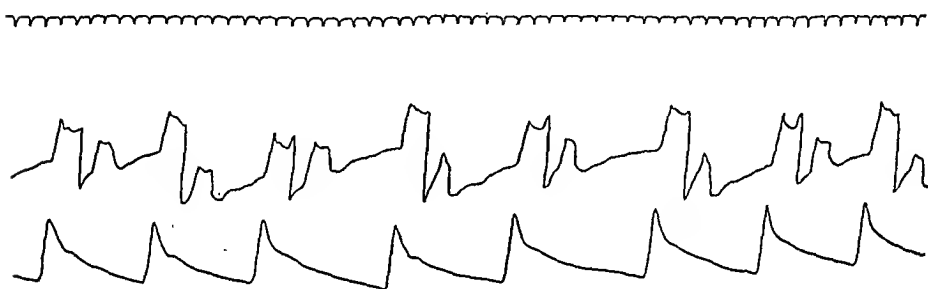


FIG. 7.—Tracing of apex beat (upper) and radial pulse (lower) in fibrillation treated with large dose of digitalis. In the apex tracing an extrasystole is seen to follow each normal beat (coupled beats or continuous bigeminus). These are too weak to cause a pulse in the radial.

In animals I have often observed auricular fibrillation occur from very large quantities of digitalis from excessive stimulation of the auricle muscle. It is of interest to note that in two cases we have met with the same phenomenon in patients. In one of these digitalis had been given for some time without slowing the pulse which maintained a rapid regular rhythm. Suddenly the rate fell to about 70 and the heart became quite irregular. All evidence of auricular activity disappeared—no *a* wave in the jugular pulse, disappearance of a presystolic murmur which was formerly present—in fact a typical picture of auricular fibrillation under digitalis was presented. With equal suddenness the fibrillation disappeared and the former rapid normal rhythm was restored, when the drug was abandoned.

Here it might be supposed is certainly an instance where the muscular action was the cause of the irregularity, for the irritability of the heart muscle is augmented by the direct action and culminates in fibrillation. I would not deny the explanation, but I may remind you that fibrillation may occur from inhibition, so that it is possible that here also the action is central.

Apart from auricular fibrillation we have met two cases in which

the rhythm was given by the auricle, but which it was quite regular though extremely rapid. In these digitalis reduced the rhythm quickly and brought relief from the dyspnoea and other symptoms. In one of them the slowing was interrupted by short phases of what seemed auricular fibrillation, but these became less frequent as the heart rate fell to the normal. The slowing of the pulse in these cases was comparable to that observed in cases of auricular fibrillation, and the question arises whether it was brought about in the same way by a diminished conduction of impulses from the auricle to the ventricle, or whether the actual discharge from the abnormal point in the auricle disappeared under the inhibitory action of the drug.

In any case the efficacy of digitalis and its allies in disorders of the heart arising from auricular hyperactivity is very striking, and raises the question whether the chief usefulness of the drug does not consist in its protection of the ventricle from the too exigent demands made on it by the auricle.

I have given you some instances in which the inhibitory factor seems to play an important, perhaps a dominant part, in the effects of digitalis in therapeutics. Let me remind you of one in which the muscular action alone is desirable. In partial or complete block the indications are to accelerate the ventricle and relieve the symptoms of arrest of the circulation which culminate in the Stokes-Adams syndrome. Bachmann, I think, was the first to utilize the muscular action of digitalis for this purpose, but it might be preferable to employ a member of the series without its inhibitory action, and in future cases I would suggest the use of helleborein or of a mixture of helleborein and digitalis.

The question as to the respective roles played by the inhibitory and the muscular factor in digitalis is not of theoretical interest only. For if the therapeutic effects are due to inhibition only, they might be elicited by other drugs which do not possess the unpleasant effects on the alimentary tract which present themselves under digitalis. On the other hand, if the muscular action is the essential factor, it might be possible to discover a drug possessing this without the inhibitory effects. In any case it seems desirable that we should be able to vary the proportions of these two factors, for there is no reason to suppose that digitalis presents the exact combination which is suitable in all cases. We, therefore, have treated a number of cases of heart disease with aconite and aconitine, which is reputed to slow the human heart by stimulation of the vagus centre, but has not the digitalis action on the cardiac muscle. But Dr. Price, who has carried out this investigation, finds that aconite does not deserve its reputation in this respect, for it failed to slow the heart even when pushed until unpleasant symptoms appeared; yet these cases afterward responded to digitalis by slowing. On the other hand, we have tried helleborein

which possesses the muscular effect of digitalis without its action on the inhibition, but the results were not satisfactory for although no slowing occurred no definite improvement followed in our cases. This may be partly owing to the fact that helleborein tends to cause diarrhoea when given in adequate doses, and we intend to continue its investigation further.

These experiences have led us to make a systematic comparison of the members of the digitalis series in therapeutics. As yet we have taken up chiefly the three common members, digitalis, strophanthus, and squills, and these we have used in the form of the tinctures, as this seemed to be of more importance than the pure principles, which are comparatively seldom employed. Our method is to give digitalis tincture first and push it until it fails to induce further improvement and unpleasant symptoms arise; then all medication is suspended for ten days or more and the patient very often relapses to his former state. Tincture of strophanthus is then given in the same way, again an interval is allowed and finally squills is prescribed; the order is not always the same of course. We have made some interesting observations for the details of which I must refer to a paper by Turnbull which will appear soon from Mackenzie's clinic. Among these I may mention that we find the tincture of digitalis (B. P.) to be nearly twice as powerful as that of squills or strophanthus, although they have been used in the same dose for many years.⁷ Both the therapeutic effects and the untoward symptoms of squills or strophanthus are only elicited when they are given in nearly twice the dose of digitalis.

In reading Withering's account of his treatment one is struck by the fact that he always induced vomiting as soon as possible and then continued his treatment with smaller doses. We have not gone so far as the pioneer, but we have found again and again that the best results are obtained only by the largest doses which can be given without gastric and intestinal symptoms. The dose which we find advisable is a dram to a dram and one-half per day of digitalis tincture, or a dram and one-half to two drams of tincture of squills or strophanthus (B. P.). This, of course, is twice as much or more than is ordinarily prescribed, and I must confess that not infrequently there arises nausea and occasionally vomiting, or sometimes severe headache from the higher dose. But on the other hand, we have patients taking a dram of digitalis per day for months and sometimes going to work under this regime.

⁷ These relations hold only for the tinctures of the B. P. The tincture of strophanthus (U. S. P.) is four times as strong as that of the B. P., and according to our results the efficient dose of this would be about one-half that of the tinctura digitalis (U. S. P.) and this is the proportionate dose actually suggested in the U. S. P. The tincture of squills (U. S. P.) on the other hand, is only one-half the strength of that of the B. P., and our results would suggest it being given in three or four times the dose of tinct. digitalis U. S. P.

There is no question that digitalis and its allies are too much feared by the medical profession. The "cumulative" action has been held over us as a bogey for so many years that many prescriptions contain this valuable drug in harmless and useless doses. *Non nocere* is a good rule, but *prodesse* is a better, and tincture of digitalis in two minim doses three times a day approaches the line of purely expectant treatment.

As regards their relative usefulness there is little difference between these three drugs. We get the same beneficial results and the same undesirable ones as regards the heart, and a patient who shows symptoms of heart block under digitalis, suffers from the same irregularity under squills or strophanthus, while when extrasystole is induced by one it follows from all. Strophanthus is often said to have less tendency to raise the blood pressure than digitalis, but in our patients neither induces any rise of pressure and in some both cause an equal fall. There is, on the whole, rather less tendency to headaches, nausea, and vomiting under strophanthus and squills than under digitalis; but the difference is not very marked and headache is caused in some cases by all three. Slight diarrhoea has followed the use of squills more than the others, and strophanthus also tends to cause this more than digitalis. This tendency to diarrhoea is still more marked from the use of helleborein and apocynum which we have begun to work upon.

In animal experiments, one of the characteristic effects of digitalis medication is the rise of blood pressure, which arises in part from the heart action, in part from a constriction of the arterioles. In patients the blood pressure is rarely augmented by digitalis and may in fact fall, as the general improvement sets in. This is, I think, due to the much greater efficiency of the vasomotor mechanism in man, which has been developed to permit of his assuming the erect attitude. As the heart fails in disease, the organ which first suffers is the brain; but anemia of the brain is promptly remedied by constriction of the abdominal vessels, by which the blood is again directed to the head areas. If, now, digitalis is given and the heart action improves, the first effect would be to increase the blood supply of the brain, and this leads the sentinel in the medulla to relax its vigilance, the mesenteric vessels are allowed to relax and the improvement in the heart may thus be coincident with lowered blood pressure. In our experience there is no significant increase in the urine except when dropsy is present.

In the course of this investigation I have been struck by the small amount of accurate knowledge that we possess as to practical therapeutics. My experience has been almost exclusively in the laboratory and perhaps I have expected too high a standard in the clinic, but in this field of cardiac tonics alone I see an endless vista of questions to be solved in the clinic if only accurate observations

are available. There seems to me to be no field in which painstaking work is more required and in which the prospects of success are more promising than in clinical therapeutics. I would commend the cultivation of this study to any one who wishes to add to the general store of medical knowledge and at the same time to devote himself to some line of work which will bear upon his own future work. But we have enough of inaccurate therapeutics already; what is needed is not a statistical compilation, but an accurate study of each individual case and a careful and, if you will, an experimental investigation of each feature presented.

PERSONAL EXPERIENCES WITH THE USE OF SALVARSAN (DIOXYDIAMIDOARSENOBENZOL, OR "606") IN THE TREATMENT OF SYPHILIS.¹

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CASE XVIII.—S. M. K., aged twenty-three years, acquired lues three years ago. Following the appearance of the secondary roseola, the patient was given a course of injections of salicylate of mercury. The injections were badly borne, causing symptoms of mercurial poisoning. From time to time mucous patches appeared in the mouth, and headache was an almost constant symptom. After a freedom from medication for more than six months, the patient was given one injection of bichloride of mercury (2 per cent., 10 minims), which was followed by bloody diarrhoea, nausea, vomiting, and salivation lasting for about a week. No further attempt at mercurial medication was made. In October, 1910, the Wassermann test was positive. In November, 1910, the patient developed mucous patches on the tonsils. The Wassermann reaction was positive. On November 15 the patient received 0.5 gram of an alkaline solution of "606" into the right buttock. The injection caused pain throughout the night following the giving of the drug, which was readily controlled by morphine. The patient was out of bed the next day, and the further course of the case was uneventful. The mucous patches on the tonsil disappeared within twenty-four hours. The patient on January 15 was free from all signs of lues. The Wasserman reaction was negative. On February 1, 1911, the reac-

¹ Concluded from page 429.

tion was again positive, although the patient is still free from all signs of lues.

CASE XIX.—P. B., aged forty-five years, had an initial lesion four months before admission. He came to the hospital with a profuse miliary syphilide over the entire trunk and extremities. He had an enormous enlargement of all the glands of the body, especially of the occipital, mastoid, preauricular and parotid, cervical, submental, submaxillary, axillary, etc. The Wassermann test was positive. On December 18, 0.6 gram of an alkaline solution of "606" was injected into the left gluteus. On December 25 the eruption on the chest and upper part of the back had, to a great extent, disappeared, and on the abdomen and back the lesions had coalesced and were desquamating. The lymph nodes were unchanged. On December 31, the day of his discharge, most of the eruption had disappeared, leaving brownish pigmented spots. On the abdomen and extremities there was still a diffuse scaliness, but no definite luetic lesions could be made out. The glands were about half their original size, but still very large. The temperature rose on the day following the injection to 101.5° , but then came down to normal. The Wassermann test was positive. On January 12 the eruption had entirely disappeared, but a general brownish pigmentation was still visible. The lymph nodes were somewhat smaller than on the previous examination, but still remained very large. The Wassermann test was positive.

CASE XX.—S. R., a housewife, aged twenty-two years, entered the hospital on December 20 after having been confined to bed for four weeks with fever, excruciating pains in the tibiae and arms, which prevented her from sleeping at night, and a pustular crustaceous syphilide on the face and back, mucous patches on both tonsils, and extreme tenderness over the bones of the forearms, wrists, and tibiae. The temperature ranged between 99° and 102° . The Wassermann test was positive. On December 22 she received 0.6 gram of an alkaline solution of "606" into the right gluteal muscle, which caused very little pain. On the night following the injection the pain over the tibiae was more severe than ever. The next day, less than twenty-four hours after the injection, the pain had left her entirely and did not reappear. There remained, however, tenderness on pressure over both tibiae for over a week. The mucous patches healed within six days. All the skin lesions disappeared within ten days, leaving pigmented spots, with the exception of two papules on the neck and forehead, which were still present on January 12. The Wassermann test on January 7 was positive.

CASE XXI.—H. M., aged twenty-three years, was admitted to the hospital on January 3, 1911, with a maculopapular syphilide, general adenopathy, and mucous patches on the tonsils and tongue; and in the middle of the latter there was a deep ulceration with a dirty base, measuring 1.5 by 1 cm. in size. The two initial lesions,

which had appeared on the penis, were present as sears. The Wassermann test was positive. Spirochetes were found in the mouth lesions. On January 3 he received 0.2 gram of "606" in liquid paraffin in the left buttock muscles. On January 4, 0.1 gram of the drug was injected in paraffin. On January 5 the patient stated that the pain in the ulcer of the tongue on swallowing had disappeared, but there was no visible change in the lesion. On January 6, 0.25 gram of the drug was injected in a similar manner. On January 8 the mucous patches on the tonsils had entirely healed and the eruption was fading. The ulcer on the tongue was clean and was healing. On January 9 he received 0.25 gram of "606" in paraffin oil as before. On January 10 the eruption had disappeared, the ulcer on the tongue was present, but was epithelializing. On January 14 the ulcer on the tongue had entirely healed and the patient was free of all manifest symptoms. The injections were almost painless, but were followed by a rise of temperature to 101° on the day after the injections. The last two injections of the drug, rubbed up in paraffin, left a marked induration, which was tender to touch. The Wassermann test on January 14 and January 21 was positive.

CASE XXII.—M. S., aged twenty-four years, contracted a chancre six months ago, for which he received thirteen injections of bichloride of mercury and two of the salicylate. He was referred to the hospital on November 15, 1910, with mucous patches on the tongue. It was thought that the lesions would yield readily to active mercurial treatment by injection, and the patient was referred to the dispensary, where he was given six salicylate of mercury injections, without any improvement. He was readmitted to the hospital on January 1 with mucous patches on the lower lip and tonsils and a hypertrophic erosion on the side of the tongue. There was also a small papule on the upper aspect of the scrotum. The Wassermann reaction was positive. On January 3, 1911, he received 0.2 gram of "606" by injection into the buttock. The drug was rubbed up with liquid paraffin. On January 4 he received 0.15 gram in paraffin in the gluteus of the opposite side. On January 6 he received 0.25 gram into the buttock. On January 8 the mucous patches on the lips and tonsils had healed and the hypertrophic papule on the side of the tongue was flat and on a level with the surface of the tongue. Epithelialization had begun. January 9 he received a fourth injection of 0.25 gram in liquid paraffin into the buttock. On January 11 all the mucous patches had healed, the papule on the side of the tongue leaving a grayish discoloration. This had disappeared by the 14th. The Wassermann reaction on January 14 was positive. Following each injection of the drug there was a rise of temperature to 101° , which quickly came down to normal. The injections were practically painless, so that it was not necessary for the patient to remain in bed.

CASE XXXI.—Mrs. M., aged forty-one years, acquired lues in September, 1908. Since that time she has had very vigorous treatment with inunctions and injections. When seen on December 10 she had relapsing mucous patches on the tip of the tongue, a circinate syphilide on the left arm, and severe headache. On December 12, 0.5 gram of an alkaline solution of "606" was injected into the left gluteus. She left the hospital on the following day, having had but slight pain. When seen again on January 6 all the lesions had disappeared, a brownish pigmentation being left at the site of the syphilide. The headaches have entirely disappeared.

CASE XLVIII.—A. K., aged forty-five years, entered the hospital in November, 1910, with a maculopapular syphilide and mucous patches. There was no history of initial infection obtainable. She was discharged after a course of injections of mercury without lesions. The Wassermann reaction was positive. In the beginning of January, 1911, she developed vertigo and dimness of vision, and upon readmission to the hospital on January 5 both vitreous chambers were diffusely cloudy, so that the disks could not be seen. Vision in the right eye was $\frac{10}{200}$, and in the left eye $\frac{6}{200}$. The diagnosis of specific chorioretinitis having been made by Dr. May, the attending ophthalmologist, the patient, on January 9, received 0.6 gram of an alkaline solution of salvarsan. The pain and vertigo disappeared within five days and the cloudiness of the vitreous chambers cleared up in a week, so that the fundi could be seen. Both fundi were found very much blurred. On January 24 the vision had improved, the right eye being $\frac{20}{30}$, the left eye, by the aid of a spherical lens—0.75 lens, $\frac{20}{70}$. The disks were still blurred. The patient had gained in weight and her general condition was improved. The Wassermann reaction was positive.

IV. *Tertiary Lesions and Gummas.*

CASE XXIII.—M. L., aged thirty-one years, and married, with healthy children, had an initial lesion six years ago. One year ago he noticed an enlargement of both testes, for which he received several series of deep injections of salicylate of mercury, with slight amelioration of the condition. The testes and epididymes on both sides were hard, nodular, and uniformly enlarged, so that the testes and epididymes could not be separated. The Wassermann test was positive. On October 16, 1910, the patient received 0.6 gram of "606" in neutral emulsion, which caused considerable pain, requiring control by morphine. On October 20 both testes were much softer and lighter in weight. On November 13 the testes and epididymes could be made out separately. The gummatous infiltration was much smaller and softer. The Wassermann test was positive. On December 4 the size of the testes on both sides was normal, but there

was left a distinct thickening of the lobus major and minor of both epididymes. The Wassermann test was positive. On January 22, 1911, the left testicle was absolutely normal. The right testicle showed a very small nodule in the upper part of the epididymes. The patient had no pain, had gained in weight, and feels better than he did in the last ten years.

CASE XXV.—S. F., aged thirty-one years, acquired an initial lesion on the penis four years ago. He came under our notice three years ago with a destructive gummatous process of the glans penis, which had resisted prolonged treatment with mercury injections. Under treatment with salicylate of mercury injections, using large doses, the gummatous ulceration of the glans penis healed, but he developed multiple gummas of the muscles of various parts of the body. Every one of these broke down while the patient was treated with salicylate of mercury injections, of which he received over seventy. About seven months ago he noticed a swelling of the left knee, with pain and difficulty on walking. This persisted in spite of the above-named treatment. At the time of his admission to the hospital he had a broken-down gumma on the buttocks, an unbroken deep gumma about the size of a horse-chestnut over the left sternoclavicular junction, and a syphilitic synovitis of the left knee-joint, with effusion obliterating the normal outlines of the joint. Wassermann reaction was positive. On October 4, 1910, he received 0.6 gram of a neutral emulsion of "606." Four hours later his temperature reached 102°, dropped then to 99°, and rose on October 8 to 102.8°; on October 11 to 104°. Simultaneously a sharply circumscribed, slightly elevated red area, 6 by 8 inches, was observed surrounding the site of the injection. A beginning erysipelas was suspected and the patient isolated. Coincidentally with the rise of temperature there occurred a diminution of the gumma at the sternoclavicular junction, and an improvement in the broken-down gumma on the buttock. The ulcer became shallower and the base cleaner. On October 12 the swelling and redness had disappeared and the diagnosis of erysipelas was abandoned. A blood examination at this time showed 8000 white blood cells and a normal differential count. The evening of this day the temperature rose to 105.4° and was accompanied by several severe chills and a follicular tonsillitis. Simultaneously with this rise in temperature there occurred marked diminution in the size of the affected knee. It was also noted that over a number of old gummas which had already cicatrized there were formed crusts, the margins became red, and on the glans penis, which was deformed by numerous scars, a serous liquid exuded from three sinuses. This modified Herxheimer reaction lasted twenty-four hours. On October 24, the day of his discharge from the hospital, the left knee-joint was normal, the ulcer on the back had healed, and the fistulous openings on the glans penis, which had been present for three years, had entirely closed. The

patient did not present himself for examination until December 15, at which time he was found to be absolutely well, had gained twelve pounds in weight, and was in perfect condition, with the function of the knee perfectly restored. On January 25, 1911, the Wassermann test was positive; his general condition was as on December 15.

CASE XXXII.—R. B., aged twenty-four years, had an initial lesion two years ago. He presented himself with cutaneous gummas over the left eyebrow, above the left ear, above the left scapula, on the right side of the lumbar spine, and on the right thigh, of about four months' duration. During the last three months he has been unable to work on account of weakness, and has lost considerably in weight. The Wassermann reaction was positive. On October 26, 0.6 gram of a neutral emulsion of "606" was injected under both scapulæ. There was considerable pain after the injection, which disappeared the next day. About one week after the injection of the drug the eruption had entirely disappeared. The Wassermann reaction was very faintly positive. There was great improvement in the general condition of the patient; he gained ten pounds in weight in two weeks.

CASE XXXIII.—I. S., aged sixty-three years, had a small lesion on the penis forty-four years ago, for which he received only local treatment. No other lesions were noticed up to the time of onset of his present trouble. For the last three months he has noticed a hard swelling on the left side of the tongue, which gives him a great deal of pain on eating and difficulty in swallowing. There was on the left border of the tongue a tumor about the size of a plum-pit, which was ulcerated on the surface. The right and left submaxillary nodes were enlarged. The Wassermann reaction was positive. On October 26, 0.5 gram of a neutral emulsion of "606" was injected in both infrascapular regions. The injection caused some pain, which was controlled by morphine. The lesion on the tongue did not show any change during the patient's five-days' stay in the hospital, nor during subsequent observation at the dispensary for four weeks. Biopsy was then made, showing the tumor to be an epithelioma, probably arising on the base of an old luetic scar.

CASE XXXIV.—G. R., aged thirty-three years, married, has four healthy children and never had any abortions. Two years ago she noticed an ulcer on the left knee, which healed in the course of a year, only to break open again. For the last year the ulcer has been gradually growing larger. Now she cannot walk on account of the lesion on the knee. Examination showed a large, irregular, serpiginous ulcer about the size of a large palm of a hand on the anterior and inner aspect of the left knee, the edges and base of which were covered with exuberant granulations, showing little tendency to epithelialize. The eye-grounds were negative. The urine was negative; the leukocytes, 8800; and the differential count normal. The Wassermann reaction was weakly positive. On October 15, 0.6

gram of "606" was injected in the subcutaneous tissue under the left scapula according to the method of Wechselsmann (neutral emulsion). Soon after the injection, and for many days thereafter, there was about the site of the injection a gradually increasing redness and some infiltration. The latter increased in size until in about a week it had assumed the size of a large lemon. There was marked tenderness, redness of the surface of the mass, and some fluctuation. Within two weeks after the injection the mass showed distinct fluctuation, broke down, and a slough of the tissues began to separate. In the course of the next month the slough gradually diminished in size, but had not completely separated under conservative measures until about two months more elapsed from the time of the injection of the drug. After the drug was injected the wound showed from the very first day evidence of healing. The progress was most marked for the first ten days, in which time more than half of the large ulcer had epithelialized. The healing was more sluggish subsequently, but within five weeks after the patient received the drug the ulcer had entirely healed. One week after the injection the Wassermann reaction was negative. The general condition of the patient improved and she gained weight. Up to the time of writing there has been no return of the ulcer. The Wassermann reaction was positive nine weeks after the injection.

CASE XXXV.—M. G., aged thirty years. No history of lues was obtainable. The patient was referred to the hospital by Dr. Abraham Jacobi with a large perforation involving the bony and cartilaginous portions of the nasal septum. The soft palate was destroyed on the right side, the uvula markedly hypertrophied and infiltrated, preventing a view of the posterior nares. The pharynx was hyperemic, with two ulcers covered with dirty gray slough. There was necrosis and hypertrophy of the epiglottis; the upper one-half was totally destroyed, the stump irregular, nodular, and thickened; and the false vocal cords were hypertrophied. There was a small ulcer on the inner side of the right calf which, on account of its appearance and its concomitance with varicose veins, was considered a varicose ulcer. The patient was hoarse and had severe pain on swallowing. The Wassermann reaction was positive. On November 7, 0.5 gram of an alkaline solution of "606" was injected into the left gluteal region. It was followed by severe pain, which lasted for twelve hours. Twenty-four hours after the injection the patient was able to eat solid food and could swallow without pain. On November 11 the pharyngeal ulcers were cleaner and smaller, and the uvula was much less infiltrated and freely movable. The temperature since the injection varied between 100.4° and 102.4°. On November 14 the pharynx was almost entirely cured, but the uvula was still thickened, though freely movable. The epiglottis showed no more induration, but still a slight grayish appearance of the stump. The patient was discharged cured on November 17.

On December 1 examination showed a normal condition of the pharynx and larynx. The small varicose ulcer, which had markedly improved while the patient was in bed, was in about the same condition as before the injection was made, confirming our original view that it was not a gumma.

CASE XXXVI.—M. V., aged thirty-nine years, has syphilis of twelve years' standing. For the past six weeks he has a painful ulcer of the soft palate. To the right of the base of the uvula there was a punched-out ulcerated area, about one-eighth of an inch deep and half an inch in diameter, covered by a dirty slough. The Wassermann test was positive. On December 7 he received 0.6 gram of an alkaline solution of "606" into the left ileocostal muscle. There was very little pain, and the patient left the hospital on December 11 with no appreciable change in the condition of the gumma. The pain, however, had entirely subsided. On December 17 the ulcer was clean and healing, with only a superficial erosion left. On December 24 the ulcer had entirely healed. The Wassermann test was positive.

CASE XXXVII.—Mrs. R., aged thirty years, contracted a very obstinate lesion on the lip about ten years ago, and has had three miscarriages and one viable foetus, with symptoms of syphilis. She has undergone repeated and strenuous antisyphilitic treatment with injections. She has now two seemingly healthy children. Since the birth of the last child, eleven months ago, she has complained from time to time of pain over the region of the liver and occasional attacks of fever. On October 19 she took to bed, and Dr. A. A. Berg, being consulted, advised an exploratory laparotomy. The liver border was found sharp and not nodular and no nodules were detected on the anterior surface of the liver, but multiple gummas were detected on the under surface. The diagnosis of gumma was confirmed by the pathologist, Dr. F. S. Mandlebaum. The pain from which the patient suffered persisted after the operation. Twenty days later the patient received 0.6 gram of an alkaline solution of "606" into the gluteal muscle. The patient left the hospital one week after the injection. Her attending physician, Dr. Morris Stark, has informed us that soon afterward the pain over the liver region disappeared entirely, and up to the time of writing she has remained free from pain. The patient states that she feels better now than ever before in her married life.

CASE XLIII.—M. P., aged twenty-eight years, was referred by Dr. Emil Mayer with the following history: A chancre was acquired eleven years ago; he was treated for one year. In November, 1910, it was found that he had a perforation of the cartilaginous septum about the size of a quarter, and of the soft palate, a painful induration over the right nasal bone, and complete obstruction of the right side of the nose, which was filled by large crusts. Upon removal of the latter a mass was seen springing from the upper portion of

the inferior turbinate, and a probe introduced into the nasal bone, showed erosion of the bone. A diagnosis of gumma of the right side of the nose, with beginning ulceration and destruction of the nasal bone, was made. A portion of this gumma was removed, and it was then seen that there was also an ulceration within the right ala. The Wassermann reaction was positive. On November 14 the patient received 0.6 gram of an alkaline solution of "606" into the gluteal muscle, causing very slight inconvenience. He left the hospital within twenty-four hours. On November 16 the tenderness over the nasal bone had disappeared. On November 28 it was found that the ulcer on the ala was entirely healed and that there was very little crust formation, no roughened edges of bone, and no sign of the gumma. The bulging appearance over the right nasal bone had disappeared and breathing was free and unobstructed. On January 4, 1911, there was no crust formation, the nasal bone was no longer painful or tumefied, and the right side of the nose was the better of the two. The Wassermann test was positive. The patient relapsed on January 11 with a destructive gumma of the septum. He lost twenty pounds in weight. He is now under treatment with mercurial injections.

CASE XLVII.—G. S., aged thirty-five years, contracted an initial lesion twelve years ago. For the last five years he has been troubled with recurring squamocircinate syphilides upon the face and trunk, for which he underwent treatment at Hot Springs (five courses of inunctions in as many years). In August, 1910, he had sixteen enesol injections. He entered the hospital on January 9, 1911, with multiple patches of a squamocircinate syphilide upon the face and trunk varying in size from a dime to a silver dollar. The Wassermann reaction was negative. On January 9 he received 0.7 gram of an alkaline solution of salvarsan. This caused severe pain, lasting a week. Ten days after the drug was given all the lesions had disappeared. The Wassermann reaction a few days after the injection was negative. This result exceeds in completeness and rapidity of action anything which we have observed after the injection of salvarsan. As to the permanence of the cure, the time elapsed since the injection is too short to permit of an opinion at this writing.

V. *Latent Syphilis.*

CASE XXIV.—F. P., aged forty-five years, acquired lues about nine years ago. For about one year following the development of secondary lesions he received treatment with protiodide of mercury in pill form and iodide of potassium. For more than seven years following this treatment the patient received no further medication, and so far as he knows there were no further lesions. About a year ago, desiring to marry, he returned to his physician for examination,

to learn whether he was free of specific taint. Physical examination was negative, but the Wassermann reaction, undertaken at this time, was positive. His physician then put him through a vigorous course of injections of bichloride and salicylate of mercury. Three Wassermann tests, taken at regular intervals, up to the time of his admission to the hospital, were successively less strongly positive, but there was still sufficient inhibition of hemolysis at the last test to call it positive. At the solicitation of the patient he was given an injection of 0.6 gram of an alkaline solution of "606" on December 24. The injection was given intramuscularly in the right buttock. It was followed by moderate pain and some stiffness, lasting about three days. Otherwise the injection was uneventful. On February 5 the patient was still free from any manifestations of lues. The Wassermann reaction was weakly positive.

VI. *Hereditary Syphilis.*

CASE XLI.—P. R., aged five years, acquired syphilis at the age of seven months from a wet nurse who was found to be syphilitic. The general eruption at that time disappeared under mercurial inunctions. Three years ago the child developed lumps on the legs and abdomen, which broke down, discharging a serous fluid. Since then he has had repeated attacks of similar lesions on various parts of the body. One year ago he began to get hoarse and became very dyspnoëic from laryngeal obstruction; this yielded to mixed treatment, but recurred six months ago and required tracheotomy. Two months ago a swelling of the left index finger and of the bone below the right elbow was noticed. The Wassermann reaction was positive. The mother gave a negative reaction. On December 23, 0.15 gram of an alkaline solution of "606" was injected into the left gluteus. On the following day an erythematous rash appeared on the body, lasting a few hours. On December 28 the swelling of the finger was much improved and the thickening of the elbow less, the measurement showing a diminution of 0.75 cm. There was considerable pain at the site of the injection, disabling the child. The temperature rose on the second day to 101.5°, and remained at 100° for two days. On January 21 the patient was able to walk without difficulty. The periostitis of the finger was almost entirely gone. The swelling of the elbow was only moderately improved.

CASE XLII.—B. S., aged fourteen years, entered Mt. Sinai Hospital on February 16, 1910, on account of swelling and tenderness over the right leg. The mother had four children and three miscarriages at three to four months; one brother has hereditary lues and has a similar swelling about his left ankle. The patient was treated with mercurial inunctions until March, 1910, without benefit. She then developed a mild mercurial nephritis, and was then treated.

with Zittmann's decoction. She left the hospital unimproved on April 6, and was subsequently treated at Mt. Sinai Dispensary by injections of mercury. No improvement took place, and she was readmitted on December 26. The anterior edge of the right tibia was broadened and presented irregularities and nodosities, the thickening continuing down to the ankle. There was marked bone tenderness. The ankle was swollen, especially on the outer side, where the normal outlines are obliterated. The skin was discolored. Pressure over the malleolus caused much pain. The diagnosis was made of periostitis and osteo-arthritis. The radiogram showed considerable absorption of the lower end of the right tibia. The Wassermann reaction, which had been negative on the first admission, became positive on January 8, 1911, after injections of mercury. On January 10 she received 0.3 gram of an alkaline solution of "606" into the gluteal muscle, followed by moderately severe pain. On January 20 she received a second injection of 0.25 gram in liquid paraffin. Following the injection the pain subsided entirely. The swelling about the malleolus has practically disappeared. The tenderness over the tibia has disappeared, although the nodules are still present.

VII. *Cerebrospinal Syphilis.*

CASE XXXVIII.—M. D., aged thirty-eight years, contracted lues eleven years ago. In May, 1910, he developed numbness and heaviness in both legs, carpet sensation under both feet, and incontinence of urine at times. The pupils reacted to light and accommodation. The knee-jerks and Achilles reflexes were absent; Romberg sign was present. He had slight ataxia of both lower extremities. He received by his attending physician, Dr. M. Radin, to whom we are indebted for these notes, thirty injections of bichloride of mercury. On September 20 there was a full ataxia of the lower extremities. On October 17 the Argyll-Robertson pupil appeared. On November 4, the Wassermann test being positive, he received 0.4 gram of an alkaline solution of "606" into the left gluteus muscle. There was slight temperature reaction, not over 101° , for the next three days. The patient was able to go about his business on the second day after the injection. On November 16 the pupils were found to react to light slightly. The subjective symptoms above enumerated improved. On November 22 a second injection of 0.45 gram of an alkaline solution of "606" was given, and caused very little pain. The patient was not confined to bed and there was no temperature rise. On December 5 the reaction of the pupils to light was more active. The reflexes were unchanged, likewise the ataxia. On December 23 the third injection of 0.45 gram of an alkaline solution of "606" was given, with no after-effects. On January 12 the knee-jerks were still absent, Romberg's sign was

present, the gait was ataxic but improved, the reactions of the pupils to light was present; the left reacted better than the right. There was great subjective improvement.

CASE XXXIX.—F. S., aged forty-one years, acquired lues twenty years ago. He had active treatment for several years. In February, 1905, diplopia, associated with frontal headaches and pain over the right parietal bone, developed. He had several attacks of diplopia, which always disappeared after active mercurial treatment. For the last eighteen months he has had almost complete freedom from ocular symptoms, but suffers from pain in the head. The patellar reflexes are always exaggerated. In the summer of 1909 he developed glycosuria and acidosis, which disappeared within a month, to reappear from time to time. In October, 1909, the Wassermann reaction was negative, but it became positive in October, 1910. On November 25 he received 0.45 gram of an alkaline solution of "606" into the buttock. Dr. F. S. Mandlebaum, who referred the patient to us for injection, has kindly informed us that the pain in the head is still present, though slightly less intense.

CASE XL.—A. S., aged thirty-six years, was seen by one of us (G.) in consultation with his family physician in 1909 and 1910. In spite of very energetic treatment with mercurial injections, he had a perforation of the hard palate. In the spring of 1910 he was confined to bed a physical wreck, unable to sit up, and seemed to be on the point of death. He was suffering from symptoms of cerebral lues. Under sixteen enesol injections, great improvement took place. There remained, however, a chain of nervous symptoms, namely, crying spells, lack of confidence to walk alone, pain in the right side of the head, dizziness, and, above all, diabetes insipidus with insatiable thirst. The patient had to drink between thirty and forty glasses of water a day, and never ventured out for even a short walk without a thermos bottle containing water. On November 21, after consultation with Dr. B. Sachs, who concurred in the diagnosis of cerebral lues, the patient was given 0.45 gram of an alkaline solution of "606" into the left gluteal muscle. The improvement in his mental condition was very slow, but the intense thirst soon subsided. The headache disappeared, but he still feels dizzy at night. The patient is now satisfied with five or six glasses of water a day. He has gained seven pounds in weight. He is able to go out accompanied, and is much more cheerful than before the injection. The inequality of the pupils has not changed, nor has the Argyll-Robertson symptom disappeared. On January 11, 1911, he received 0.3 gram of "606" in paraffin emulsion.

CASE XLIV.—S. F., salesman, aged forty-six years; does not remember primary luetic infection. Five years ago he developed an intranasal lesion, which was diagnosticated as a gumma. This yielded readily to antispecific treatment, but recurred two years later for a short time. For the last few years he has had attacks

of hemiplegia or numbness of the left side, associated with loss of consciousness, and involuntary urination and defecation, lasting one to seven days, and gradually subsiding. In the interval between these attacks his memory, previously good, frequently lapses. Two years ago he had an attack of arthritic pain, which yielded to antispasmodic treatment. He has received from his physician a very large number of mercurial injections and much potassium iodide. The patient responded intelligently to questions. His pupils were slightly unequal in size, but reacted normally to light and accommodation. His eye-grounds were practically negative. His reflexes were much exaggerated and his gait showed a slight weakness of the left leg, but no ataxia. The physical examination otherwise was negative. He is rather dull and stolid mentally. The Wassermann test was negative. On December 20, 1910, the patient received into the right buttock muscles 0.6 gram of "606." Aside from slight immediate pain, the patient did not have any further pain or stiffness. There was no temperature reaction. The patient was observed for four days in the hospital and subsequently by his physician. There was no change noted for the better in his mental state. On January 15 the patient was less emotional. He shows more energy and takes interest in his business affairs.

TABULAR SYNOPSIS OF THE CASES.

Case No.	Infection.	Lesion.	Treatment.	Wassermann.	Injections of "606."	Date.	Result.	Subsequent Wassermann.	Remarks.
I H. J.	4 weeks	Chancre (spirochete present) and inguinal adenitis	None	Positive (weakly)	0.6 gram alkaline solution	Dec. 20	Chancre healed on Dec. 31	Wassermann strongly positive, Dec. 31; negative, Jan. 12	On Feb. 3 no secondaries.
II R. S.	17 days	Chancre (spirochete present) (herpetic)	None	Negative	0.6 gram alkaline solution	Dec. 24	Chancre healed in 3 days	Wassermann positive, Dec. 5, negative	No secondaries Feb. 5.
III C. P.	2 months	Chancre and maculopapular syphilide and mucous patches	None	Positive	0.6 gram alkaline solution	Jan. 6	Eruption cured in 1 week	Jan. 20, weakly positive	Patient gained 4 pounds in 1 week.
IV M. N.	2 months	Chancre (spirochete present and secondaries)	2 injections of Hg. Sal.	Positive	0.6 gram alkaline solution	Jan. 13	Chancre cured in 2 weeks	Severe pain and extreme nervousness for 1 week after injection; diffuse erythematous eruption.
V J. C.	5 months	Chancre on left tonsil; mucous patches; spirochete present	None	Positive	0.4 gram neutral emulsion	Sept. 26	Cured in 1 week	Positive, Oct. 3, Dec. 19, Jan. 8	Necrosis at site of injection.
VI A. Y.	2 months	Macular syphilide; mucous patches and condylomas	None	Positive	0.4 gram neutral emulsion; 0.6 gram alkaline solution	Sept. 28 Jan. 2	Cured in 11 days Relapse Dec. 27 Cured in 40 days	Oct. 28, faintly positive; Nov. 1-7, negative; Dec. 5, positive; Jan. 8, positive	Necrosis; relapse after 2½ months; total amt. "606" = 1 gram.
VII P. E.	3 months	Maculopapular syphilide; mucous patches; iritis (spirochete present)	None	Positive	0.45 gram neutral emulsion	Oct. 8	Cured in 6 days	Oct. 29, positive; Nov. 12, positive (weakly)	Marked Herxheimer reaction; nerve palsies; see case history.
VIII J. M.	8 months	Maculopapular syphilide; mucous patches; condylomas (spirochete present)	Mixed treatment, few months	Positive	0.5 gram neutral emulsion	Oct. 25	Cured in 9 days	Nov. 15, positive (weakly); Dec. 24, negative; Jan. 20, positive	Rapid cure; gain of 20 pounds in 2 months.
IX F. K.	About 1 yr.	Gumma pharynx; malignant syphilis	Numerous injections and injections of Hg.	Positive	0.6 gram neutral emulsion	Oct. 21	Cured in 23 days	Nov. 13, positive	Case uninfluenced by Hg. and KI; cured quickly by "606"; local necrosis at site of injection.
X M. O.	2 months	Maculopapular syphilide; mucous patches; spirochete present in healing chancre	None	Positive	0.5 gram neutral emulsion	Oct. 26	Mucous patches cured in 4 days Rosacea cured in 14 days	Nov. 16, positive	Gained 20 pounds in 3 weeks.

XI. C. S.	15 months	Periostitis tibia	Numerous in- jections and None	in-Positive	0.6 gram neu- tral emulsion	Nov. 1	Cured in 3 days	Nov. 11, positive; Jan. 13, positive.
XII G. S.	Indefinite	Chancre on right tonsil; maculopapular syphilide; condylomas; mucous patches (spirochete present)	None	Positive	0.45 gram neutral emulsion; relapse; 0.6 gram alkaline solution	Oct. 3 Nov. 10	Cured in 17 days Relapse Nov. 9 Cured in 14 days	Oct. 24, negative; Nov. 7, negative; Nov. 12, positive Marked Herxheimer reaction, lasting 24 hours; gravid; fetus viable Nov. 10.
XIII F. G.	2½ months	Pustular syphilide; mucous patches (spirochete present); malignant case	6 injections Hg. Cl ₂	of Positive	0.6 gram alkaline solution	Nov. 11	Cured in 8 days	Nov. 19, positive; Jan. 1, faintly positive
XIV C. W.	11 months	Mucous patches (spirochete present)	27 injections of Hg. Sal.	of Positive	0.6 gram neutral emulsion	Oct. 5	Cured in 2 days Relapse 3 mos. later; squamous palmar syphilis	Oct. 10, positive; Nov. 1, positive; Nov. 13, positive (weaker) Feb. 5, negative Relapse, Feb. 5
XV H. B.	8 months	Mucous patches (spirochete absent)	70 injections of Hg.	of Positive (weakly)	0.6 gram alkaline solution	Nov. 11	Cured in 4 days	Dec. 4, positive.
XVI F. K.	2 months	Intra-urethral chancre; roseola; mucous patches; spirochete absent	None	Positive	0.6 gram neutral emulsion	Oct. 7	Cured in 8 days	Nov. 30, weakly positive; Dec. 23, positive Feb. 5, positive
XVII L. S.	1 year	Mucous patches	15 injections of Hg. Sal.	of Positive	0.5 gram alkaline solution, intravenously	Dec. 2	Lesions disappeared in 2 days; death 2 weeks after injection	See history.
XVIII S. M. K.	3 years	Mucous patches; no spirochete found	Hg. injection; KI	Positive	0.5 gram alkaline solution	Nov. 15	Cured within 24 hours	Positive, Dec. 1; negative, Jan. 15; positive, Feb. 1
XIX P. B.	4 months	Miliary syphilide; adenitis	poly-None	Positive	0.6 gram alkaline solution	Dec. 18	Syphilide disappeared in 3 weeks; adenitis uninfected	Positive, Jan. 12 Adenitis resistant to "606"; infiltration at site of infection.
XX S. R.	?	Pustulocrustaceous syphilide; mucous patches; periostitis	None	Positive	0.6 gram alkaline solution	Dec. 22	Mucous patches cured in 6 days Skin lesion cured (?) in 10 days	Two papules on face uninfuenced by drug.
XXI H. M.	2 months	Roscola; mucous patches	None	Positive	0.8 gram paraffin emulsion	Jan. 3-9	Cured in 11 days	Positive, Jan. 14-21
XXII N. S.	6 months	Mucous patches	15 injections of Hg. Sal.; 8 injections of HgCl ₂	of Positive	0.85 gram paraffin emulsion	Jan. 3-9	Cured in 11 days	Positive, Jan. 14 Drug given in divided doses; no pain. Drug given in divided doses; slight pain; lesions refractory to Hg.

TABULAR SYNOPSIS OF THE CASES—(Continued).

Case No.	Infection.	Lesion.	Treatment.	Wassermann.	Injections of "606."	Date.	Result.	Subsequent Wassermann.	Remarks.
XXIII M. L.	6 years	Bilateral orethritis	Numerous Hg. Sal. injections	Positive	0.6 gram neutral emulsion	Oct. 16	Cured in 6 weeks	Positive, Dec. 4	
XXIV F. P.	9 years	None	Internal and injections of Hg.	Positive	0.6 gram alkaline solution	Dec. 24	Positive (weaker), Jan. 15	At patient's request before marriage.
XXV S. F.	4 years	Multiple gummas; synovitis	Prolonged Hg. Sal. injections, and KI	Positive	0.6 gram neutral emulsion	Oct. 4	Cured in 20 days	Positive (weaker), Jan. 24	Case refractory to Hg.; modified Herxheimer reaction; temperature, 105.4°; follicular tonsillitis after injection.
XXVI G. P.	Indefinite	Gumma (?) of left shoulder; paralysis of both vocal cords	None	Negative	0.5 gram paraffin emulsion	Jan. 16- Jan. 18	Improved.	Patient had been operated on twice; wound refuses to heal; injected at request of surgeon.
XXVII H. M.	4 years	Gumma submaxillary region	Injection of "606" at another institution 2 months ago; injections and injections	Negative	0.75 gram paraffin emulsion	Jan. 16- Jan. 20	Considerable improvement.	Injected at request of surgeon.
XXVIII G. D.	4 years	Chronic nasal catarrh; old specific soars; deafness	Injections and KI	Positive	0.55 gram paraffin emulsion	Jan. 18- Jan. 20	Hearing greatly improved	At end of 5 days could hear watch tick at 1 foot; before could not hear conversation.
XXIX J. S.	2 months	Healing chancre; mucous patches; neuritis	Internal Hg. 2 months ago	Positive	0.55 gram paraffin emulsion	Jan. 17- Jan. 23	Cured in 1 week	Mercurial nephritis before "606"; urine still contains casts.
XXX A. B.	Indefinite	Paresis	Unknown	Positive	0.6 gram alkaline solution	Dec. 11	Unimproved.	
XXXI Mrs. M.	2 years	Mucous patches; headache; circinate syphilide	Inunctions and injections	0.5 gram alkaline solution	Dec. 12	Cured in 24 days		
XXXII R. B.	2 years	Multiple cutaneous gummas	Hg. injections	Positive	0.6 gram neutral emulsion	Oct. 26	Cured in 1 week	Positive (weak), Nov. 9	Gained 10 pounds in 2 weeks.
XXXIII I. S.	44 years	Epithelioma of tongue	None	Positive	0.5 gram neutral emulsion	Oct. 26	Unimproved	Negative, Jan. 15	Biopsy shows epithelioma; radical operation confirmed diagnosis.

XXXIV G. R.	Unknown	Gummatous ulcer of knee	Injections of Hg.	Positive (weakly)	0.6 gram neutral emulsion	Oct. 15	Cured in 5 weeks	Oct. 22, negative; Dec. 23, positive	Large necrosis at site of injection.
XXXV M. G.	Unknown	Gummas of nose, soft palate, and pharynx	Mixed treatment	Positive	0.5 gram alkaline solution	Nov. 7	Cured in 10 days	Immediate improvement of pain and difficult swallowing
XXXVI M. V.	12 years	Gumma of soft palate	Hg. injections	Positive	0.6 gram alkaline solution	Dec. 7	Cured in 2 weeks	Dec. 24, positive.	
XXXVII Mrs. R.	10 years	Gummas of liver	Injections	0.6 gram alkaline solution	Nov. 8	Cured in 3 weeks	Diagnosis confirmed by exploratory and biopsy.
XXXVIII M. D.	11 years	Tabes	Hg. injections	Positive	1.3 grams alkaline solution	Nov. 4	Subjective improvement	Ataxia unchanged; Argyll-Robertson pupil gone.
XXXIX E. S.	20 years	Cerebrospinal lues	Hg. injections	Positive	0.45 gram alkaline solution	Nov. 22	Improved; headache gone.		
XL A. S.	4 years	Cerebral lues; incipient paresis	Hg. injections	0.75 gram alkaline solution and paraffin emulsion	Nov. 21	Unimproved.		
XL P. R.	4 years	Hereditary lues	Hg. injections; mixed treatment	Positive	0.15 gram alkaline solution	Dec. 23	Much improved.		
XLII B. S.	14 years	Hereditary lues	Injections, injections, and KI	Positive	0.55 gram alkaline solution and paraffin emulsion	Jan. 10	Much improved.		
XLIII M. P.	11 years	Gumma of nose	Hg. for 1 year	Positive	0.6 gram alkaline solution	Nov. 14	Gumma cured in 2 weeks; relapse Jan. 11	Jan. 4, positive	Lost 20 pounds; put on Hg. injections.
XLIV S. E.	Unknown	Paresis	Numerous Hg. injections	Negative	0.6 gram alkaline solution	Dec. 20	Unimproved.		
XLV L. M.	2 years	Mucous patches	Injections and injections	0.7 gram paraffin emulsion	Jan. 21	Improved.		
XLVI E. L.	20 years	Pachymeningitis	Hg. injections for 20 years	Positive	0.4 gram paraffin emulsion	Jan. 19	Improved.		
XLVII G. S.	12 years	Squamous eircinate syphilide	Hg. injections and encesol injection	Negative	0.7 gram alkaline solution	Jan. 9	Cured in 10 days	Negative, Jan. 16	
XLVIII A. K.	Indefinite	Chororetinitis in secondary	Hg. injections	Positive	0.6 gram alkaline solution	Jan. 9	Improved markedly in 10 days	Positive, Jan. 16	Feb. 7, eyesight nearly normal

THE PHYSIOLOGY OF THE PITUITARY GLAND AND THE ACTIONS OF ITS EXTRACTS.¹

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LODGED in the saddle of the sella turcica and shielded in a privileged manner from the traumatisms of the outside world, lies a small body, the hypophysis cerebri, or pituitary gland, the function of which has always been, and still is, largely shrouded in mystery. Since Galen and Vesalius taught that it filtered mucus into the nose and pharynx, the functions attributed to this gland have varied from such vitalistic conceptions as a habitation for the soul or a stopper preventing the escape of vital spirits from the third ventricle, to the more lowly duties of an excretory organ for the brain, a lymphatic gland, etc. Obviously, no scientific conception of the organ's function could be formulated until its development and structure were understood and, consequently, the discovery of its dual origin in 1838 by Rathke² marks the time when a beginning could be made toward the unveiling of its true function. Since then a host of histological investigators, prominent among them, Stieda,³ Schönemann,⁴ Müller,⁵ Schwalbe,⁷ Berkley,⁷ v. Kölliker⁸ Paulesco,⁹ and Herring,¹⁰ have added in a material manner to a clear understanding of its structure and development.

HISTOLOGY AND EMBRYOLOGY. The pituitary body consists of a large pink-colored anterior portion, and a smaller pale posterior part. Developmentally considered, the posterior lobe arises as a downward growth from the midbrain, its cavity being continuous with the third ventricle. This part remains permanently connected with the brain by a stalk or infundibulum, the cavity of which, except in the cat, becomes obliterated by a growth of neuroglia tissue. The anterior portion arises as an upgrowth from the buccal ectoderm, which is cut off by the fusion of the sphenoidal cartilages. At first this cut-off mass exists as a hollow island of cells, but as the cells proliferate only a cleft remains. The cells on the posterior side of this cleft apply themselves to the posterior lobe, which they cover and invade to some extent, forming cut-off masses

¹ Presented before the Detroit Medical Club, June 2, 1910.

² Müller's Archiv., 1838, p. 482.

³ Ztschr. f. wissenschaft. Zoologie, 1868, xviii, 44.

⁴ Arch. f. path. Anat. u. Physiol., 1892, cxxix, 310.

⁵ Ztschr. f. Naturwissenschaft., 1891, vi, 354.

⁶ Referred to by Herring (Ref. 8).

⁷ Brain, 1894, xvii, 515; Johns Hopkins Hosp. Reports, 1895, iv, 285.

⁸ "Entwicklungsgeschichte," 1878.

⁹ Quoted by Parhon and Golstein, "Les Secretions Internes," Paris, 1907.

¹⁰ Quart. Jour. Exp. Physiol., 1908, i, 121.

of cells. The rest of the cells develop into the large anterior lobe, which becomes very vascular.¹¹

When fully developed, the posterior lobe is composed of neuroglia tissue, together with a few ependymal cells. Berkley believed he observed also nerve cells and fibers, but this has not been substantiated by subsequent investigators, and it seems probable, as Herring points out, that the cells described as nerve cells were in reality not such. The posterior lobe has an epithelial investment, first described by Peremeschko,¹² in 1867, but more in detail by Paulesco, in 1906, and Herring, in 1908. According to this latter observer, the completeness of this epithelial covering varies in different animals. In the cat and dog the investment is complete, but in most mammals (man, monkey, ox, pig, rabbit) the epithelium does not entirely surround the posterior lobe, but is more particularly gathered toward its anterior part, forming the *pars intermedia* of the pituitary gland. A few gland cells are seen scattered here and there throughout the neuroglia tissue. This part is almost devoid of bloodvessels, and the colloidal secretion (or degeneration products?) of the epithelial cells is passed into the neuroglial tissue to be absorbed, by its lymphatic system, into the third ventricle.

The anterior lobe consists largely of differentially staining, granular cells, that are arranged in columns around thin-walled blood spaces. No evidences of glandular ducts are present. Haller¹³ claims that the anterior lobe is a tubular gland, discharging its secretion directly into the subdural space, but the evidence of other histologists appears against such a view, and indicates rather that these cells discharge their secretion directly into the blood spaces.

THE FUNCTIONS OF THE PITUITARY GLAND. One of the first questions of interest in studying a gland's function is its necessity to life. Physiologists and surgeons alike have attempted to answer this question by determining the effects of its removal. In 1892 Marinesco¹⁴ reported that removal of the pituitary gland in cats was fatal within one to eighteen days after the operation. Before death the animals showed signs of emaciation, a fall in temperature and heart rate. Vassale and Sacchi¹⁵ reported that the removal of the pituitary gland in forty animals (cats and dogs) resulted in death within five to seven days. The symptoms before death consisted in an accelerated respiration (amounting at times to dyspnoea), polyuria, polydipsia, vomiting, rigidity of the posterior limbs, fibrillary twitchings and clonic as well as tonic convulsions. Partial removal caused less pronounced symptoms, and occasionally the animal survived. Similar results have been reported by Casselli.¹⁶

¹¹ For excellent diagrams see Herring, *Quart. Jour. Exp. Phys.*, i, 121.

¹² *Arch. f. path. Anat. u. Physiol.*, 1867, xxxviii, 329.

¹³ *Morpholog. Jahrb.*, 1896, xxv, 101.

¹⁴ *Compt.-rend. Soc. de biol.*, June, 1892.

¹⁵ *Arch. ital. de biol.*, 1893, xviii, 3.

¹⁶ Quoted by Parhon and Golstein (*loc. cit.*).

In 1900 Friedmann and Maas¹⁷ reported that extirpation of the pituitary gland was compatible with life. Lo Monaco and Van Rynberk,¹⁸ in 1901, Gaglio¹⁹ in 1902, and Pirrone²⁰ in 1903, also came to this conclusion. They admitted that serious symptoms and even death often followed its removal, but attributed these unfortunate events to cerebral traumatism or infections. The fact that some animals survived fifty to eighty days was advanced as proof sufficient that the gland was not of vital importance. In 1905 Fichera²¹ found that partial removal of the gland in pullets caused, not death, but a stunted growth. He could not be certain; however, that the effects were not due to cerebral injury.

Experimenters were thus divided into two camps, the one group believing that the gland was of vital importance, suspicioned an incomplete removal in case death failed to occur; the other group holding that it was not necessary to life, attributed the symptoms and death to cerebral injury and infection. This was the state of affairs in 1906 when Paulesco²² devised the technique for the temporal route of reaching the pituitary body, a method that possesses at least two advantages, viz.: it permits the removal of the gland *de visu* and minimizes the risk of infection or traumatism. Paulesco²³ reported that complete removal by this method was invariably fatal, but that partial removal was compatible with life if the part remaining contained some of the anterior or epithelial portion. Cushing,²⁴ in this country, has been able by the use of this method to substantiate that ablation of the anterior lobe is always fatal in adult canines, but that removal of the posterior lobe is entirely without effect. Crowe and Cushing²⁵ point out, however, that young animals survive a total hypophysectomy longer than adult ones. Crowe, Cushing, and Homans²⁶ have strengthened these results by being able to ward off death and the serious symptoms caused by total extirpation of the gland, by its transplantation into the brain substance or the red bone marrow of long bones.

Not only is the gland necessary to sustain life, but clinical men and pathologists have also added evidence which indicates its importance to normal functions, for, when the anterior lobe becomes hypertrophied or atrophied (implying increased or decreased secretion), certain developmental disturbances apparently arise which vary in degree at least with the age at which they occur. Thus, a congenital hypertrophy of the pituitary gland is frequently asso-

¹⁷ Berl. klin. Wehnschr., 1900, p. 1213.

¹⁸ Quoted by Parhon and Golstein (*loc. cit.*).

¹⁹ Arch. ital. de Biol., 1902, xxxviii, 177.

²⁰ Quoted by Parhon and Golstein (*loc. cit.*).

²² Report at Acad. des science., June, 1907; "L'Hypophyse du Cerveau," 1908.

²³ *Loc. cit.*

²⁴ Proc. Amer. Physiol. Soc., Amer. Jour. Physiol., 1908, xxiii, 23.

²⁵ Jour. Amer. Med. Assoc., 1909, liii, 247.

²⁶ Quart. Jour. Exp. Physiol., 1909, ii, 389.

²¹ *Ibid.*

ciated with a general overdevelopment of the body (giantism), whereas an hypertrophy occurring in adult life apparently gives rise to acromegaly, a condition characterized by greatly overdeveloped extremities. Congenital hyposecretion causes infantilism, whereas later in life it is followed by a loss of sexual characteristics. These altered states of secretory activity may be induced by various causes, some but imperfectly understood. The compression of the pituitary by tumors, the effect of blood supply and nutrition and of the products elaborated by other glands of internal secretion on the pituitary are still awaiting more detailed investigation and need concern us here no further.

The following facts, then, seem established: (1) The pituitary gland is necessary to life, and any diminution or increase in its function results in metabolic or sexual disturbances; and (2) this control over the body is probably exerted through an internal secretion elaborated *by the cells of the anterior lobe*.

NATURE OF THE INTERNAL SECRETION. Has the internal secretion been determined? What is its nature? Is it a single substance or does the gland secrete a number of substances? Answers to these and similar questions have been sought by studying the effects of injections of its extracts on the muscular and nervous functions, on nutrition and development, on the secretion and composition of urine, on the flow of the digestive juices, and on the cardiovascular system, this latter supplying the most productive field for research.

Experimentation has shown that by water, glycerine, or salt solutions, a substance may be extracted from either fresh or dried glands which resist boiling, and, when introduced intravenously or intraperitoneally, causes polyuria, slow or accelerated pulse, accelerated respiration, dyspnoea and motor disturbances, such as ataxia and paralysis of the hind legs, symptoms, it will be noted, which are also characteristic of the removal of the gland. This substance is obtained only from the posterior lobe, however. The extracts thus far obtained from the anterior lobe are apparently inert even when injected in enormous doses.²⁷ This fact seems very peculiar since it is the anterior lobe which is composed of glandular tissue and which would, therefore, be expected to furnish the physiologically active principle, and the paradox becomes still more interesting when we consider that it is this portion alone which is of vital importance.

The fact may receive several interpretations. We may imagine that the active substance is secreted by the anterior lobe in an inactive form and that it becomes activated or chemically altered in some manner as yet not understood after reaching the posterior or neuroglial portion. Schäfer²⁸ apparently leans toward such a view. This hypothesis, nevertheless, requires a brave assumption, since,

²⁷ L'Hypophyse et la Medication hypophysaire, Paris, 1909.

²⁸ Philosoph. transact. B., c. 1.

first, no proof exists that neuroglial tissue possesses such an activating or formative power; and, secondly, there is no evidence that the anterior lobe passes its secretion into the posterior lobe—in fact, histological evidence appears opposed to it. For this reason, it seems to me, we are not justified in assuming that the substance extracted from the posterior lobe is identical either in composition or action with that of the anterior lobe. Until further evidence is forthcoming, I prefer to believe that this lobe elaborates a secretion as yet unknown, which affects nutrition and is necessary to life, and that the posterior lobe either forms an additional secretion not of vital importance, or contains chemical substances which, though not normally secreted into the blood, when extracted and introduced, affect the body functions. The reasons for my belief, summarized, are: (1) The anterior lobe alone has an influence on growth, development and life, whereas the extracted substance is found only in the posterior lobe; (2) there is no evidence of the extracted substance in the normal circulation; and (3) injections of the extract do not neutralize the symptoms arising from extirpation of the gland, but, in large doses, they produce symptoms that simulate them.

For the present, then, it seems preferable to regard *extracts of the pituitary gland* rather as drugs which exert a characteristic action on the body than as physiological secretions—drugs whose therapeutic value consists of the effects they may produce on the heart, bloodvessels, kidney, etc., rather than of any hypothetical value they may possess in supplementing a deficient function of the anterior lobes.

THE ACTIONS OF PITUITARY EXTRACTS (SOME UNSETTLED PROBLEMS). A perusal of the literature indicates that the effect of pituitary extracts, even on the circulatory system, where it has been most extensively studied, is by no means universally agreed upon. To expedite an analysis of its action, I have summarized the literature on its circulatory effects and in the discussion propose to add a number of results that I have recorded while using pituitary extract in investigating other problems (Table I).

TABLE I.—Summary, *Circulatory Effects of Pituitary Extracts.*

Investigator and date.	Portion used.	Solvent or extractive.	Effect on blood pressure.	Effect on heart rate.	Effect on amplitude of beat.	Action on bloodvessels.	Remarks.
Oliver, Schäfer, 1895 Howell, 1898	Entire gland Anterior lobe Posterior lobe	Water, glycerine Water, glycerine	Increased No effect Increased	No slowing No effect Slowed	Increased { Increased or decreased Increased	Constriction Constriction	Vagotomy modified slowing Vagotomy prevented slowing
Livon, 1898	?	Glycerine	Increased	Slowed	Increased	Constriction	Vagotomy abolished slowing
Schäfer, Vincent, 1899	Anterior lobe Posterior lobe Posterior lobe	Saline Alcohol	No effect Increased on 2d or 3d Injections decreased Decreased	No effect No effect or slowed	Increased	Constriction	Slowing not entirely prevented by atropine or vagus section
de Cyon, 1899-1900	Entire gland (?)	Alcohol Saline	Increased Fell	Slowed; periodic rhythm Slowed	Increased	Constriction Dilation	
Osborne, Vincent, 1900	Posterior lobe (outer part) Posterior lobe (inner part) Anterior lobe	Alcohol Salt solution Salt solution	Negative Increased	Slowed or no effect Increased	Decreased		
Hamburger, 1904-1910	Anterior lobe Posterior lobe	Saline, alcohol, glycerine Salt solution Salt solution	Decreased Negative Temporary increase Later, decrease	Increased Later decreased		
Silvestrini, 1905	Anterior lobe Posterior lobe	Salt solution Salt solution	Negative Negative		
Garnier, Thonon, 1906	Anterior lobe Colloid at anterior lobe Posterior lobe Anterior lobe	Salt solution Salt solution Salt solution Salt solution	Increase Later decreased Negative	Slowed	Increased Weaker	Vagotomy prevents slowing
Schäfer, Herring, 1906	Entire gland (?)	Saline	Increased	Slowed	Constriction, later dilation Constriction	
Halliburton, Carrion, 1907	Epithelial portion posterior lobe Neuroglial portion	Saline Saline	Increased Decreased on subcutaneous injection	Slowed or no effect Often temporary acceleration		
Schäfer, Herring, 1908	Same ?	Alcohol ?	Increased	Slowed	Increased	Slowing not abolished by vagotomy
de Bonis, 1908							
Halliburton, Candler, Sikes, 1909	Posterior lobe (human pituitary)	Saline	Increased	No effect			

Effects on Bloodvessels and Arterial Pressure. Experimenters are commonly agreed that pituitary extracts cause a rapid and pronounced increase in blood pressure, different from that of adrenalin in its longer duration. This rise is largely due to a constriction of the arterioles, for, as shown by Oliver and Schäfer,²⁹ Howell,³⁰ and later by Schäfer and Vincent,³¹ the size of organs such as the intestine, spleen, and limbs diminish concomitantly with the elevation of pressure. The constrictor action is chiefly peripheral, for, as Oliver and Schäfer, and also Howell, have demonstrated, it occurs after destruction of the medulla and spinal cord. Furthermore, Oliver and Schäfer found that it decreased the flow through a perfused frog. More recently, Magnus and Schäfer³² have supplied evidence that not all the peripheral vessels are affected equally, and have pointed particularly to the frequent and prompt increase in size of the kidney when the pressure rises, an effect directly opposite to that produced by adrenalin. While investigating the relative value of vasomotor drugs in renal hemorrhage,³³ I had occasion to substantiate this fact, and further, to show that the venous outflow from this organ was markedly augmented after administration of pituitary extract. These results indicate either that the rise in pressure passively overpowers the local constriction or that the drug exerts a direct dilator action on the renal vessels as well. I have a number of times perfused the drug through the kidney of a dog and when thus tested invariably caused a constriction, as shown by a decreased outflow and an increase in the height of the oscillatory perfusion pressure. The constriction induced by the extract obtained from $\frac{1}{10}$ gram of fresh infundibulum corresponded in degree to that resulting from 1 c.c. of a 1 to 100,000 solution of crystalline adrenalin. From this it differed, however, by being of *shorter duration* and unmodified, as far as I have been able to determine, by a dose of apocodein or of ergotoxin sufficient to abolish completely the action of adrenalin. Should subsequent experiments corroborate this observation, it would indicate that the drug acts directly on the muscle and not on the nerve endings in the bloodvessels, as is the case with adrenalin. In a few cases the constriction induced by pituitary extract was followed by a dilation such as I have previously reported following the constriction of chloroform. Such a dilation has not only been obtained with the commercial preparation "Pituitrin," in which the chloretone preservative might possibly be suspected of being responsible for the dilation, but with a saline extract of the fresh infundibular portion containing no preservative. It is not impossible that a larger series of perfusion experiments

²⁹ Jour. Physiol., 1895, xviii, 277.

³⁰ Jour. Exp. Med., 1898, iii, 248.

³¹ Proc. Physiol. Soc., Jour. Physiol., 1899, xxiv; Proc. of Soc., p. xix; Jour. Physiol., 1900, xxv, 87.

³² Jour. Physiol., 1901, xxiii; Proc. Soc., 9.

³³ Arch. Int. Med., 1910, v, 348.

on various organs may show this dilation frequently to follow the preliminary constriction thus indicating that the increase in the kidney volume observed in animal experiments is not entirely a passive affair. Sollmann has also shown that pituitary extract has a slight central dilator action, for when the spleen left in contact with the central nervous system was perfused, an intravenous injection caused a slight dilation of the splenic vessels.

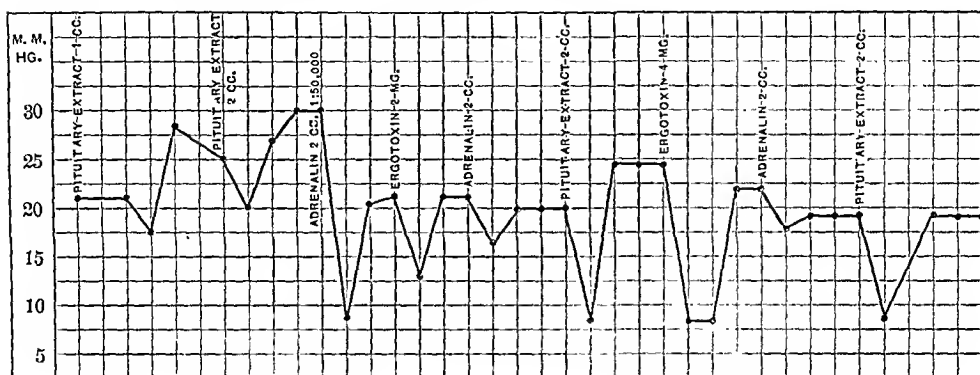


FIG. 1.—Plot showing action of pituitary extract and adrenalin when perfused before and after ergotoxin.

Action on the Heart. Most experimenters have come to the conclusion that pituitary extract slows the heart and increases the amplitude of its contractions, but the details are more or less at variance. Oliver and Schäfer³⁴ in their first report observed no changes in heart rate, but Howell³⁵ described a slowing which occurred synchronously with the main rise in pressure. Schäfer and Vincent³⁶ subsequently observed this slowing, but found it entirely absent in a certain number of cases. When it did occur, it was usually not coincident with the rise of pressure, but occurred after the pressure had passed the highest level. Not infrequently, too, it was preceded by a period of acceleration. Similar differences in results are also evident in the reports and curves of other investigators. In addition to a slowing, de Cyon³⁷ and Garnier and Thaon³⁸ noted changes in the rhythm of the heart, the beats grouping themselves into periods of two or more.

The causation of the slowing is also unsettled. According to Livon,³⁹ Garnier and Thaon,⁴⁰ and Schäfer and Vincent, it is apparently due to a stimulation of the cardio-inhibitory centre, since it is abolished by vagus section. According to Howell and de Cyon it is at least only partly due to this, for, while the cardiac action may

³⁴ Loc cit.

³⁶ Loc cit.

³⁷ Arch. f. d. ges. Physiol., 1898, lxxiii, 339; 1900, lxxxi, 94.

³⁸ Jour. de physiol. et de path. gén., 1906, viii, 251.

³⁹ Jour. de physiol. et de path. gén., 1909, ix, 16.

³⁵ Loc cit.

⁴⁰ Loc cit.

be modified by the section of the vagi, or by injection of atropin, slowing is not prevented. They, therefore, concluded that pituitary extracts exert a direct effect on the heart as well. Support is given to this view by the fact that the same slowing occurs, as I have found, when the drug is perfused through a rabbit's heart isolated from all nerve centres. In such experiments the peculiar grouping of beats was also occasionally present.

As far as the effect of intravenous injections on heart rate is concerned, I find that my records of twenty-seven injections consist of a miscellaneous series of results corroborative of nearly every worker. The same pituitary extract (Pituitrin, P., D. & Co.) was employed in all of these cases.

TABLE II.—*Effect of Pituitary Extract on Rate and Contraction of Heart.*

Experiment.	Dose pituitrin.	Rate per 10 sec.			Amplitude in mm.			Remarks.
		Before.	During pressure rise.	1 minute after.	Before.	During pressure rise.	1 minute after.	
327	2 c.c.	21	..	17	18	18	17	
329	2 c.c.	17	..	15	11	12	9	
330	2 c.c.	18	..	15	16	16	14	
	4 c.c.	17	..	15	16	16	14	
333	2 c.c.	20	23	20	12	16	11	
335	2 c.c.	29	29	24	20	18	15	
334	2 c.c.	31	..	30	18	..	13	After hemorrhage
339	4 c.c.	34	30	21	24	26	9	Vigorous artificial respiration
341	2 c.c.	27	27	20½	10	12	11½	After hemorrhage
355	2 c.c.	18	17	18	22	20	19	
	3 c.c.	18	18	18	14	14	13	
	4 c.c.	16	17	16	14½	14½	14	
360	4 c.c.	16	15	15½	25	25	27	
361	3 c.c.	23	22	20	17	14	15½	
	3 c.c.	22	22	22	17½	18	18½	After atropine, 1 mg.
	4 c.c.	17	16	16	17	18	16½	
362	3 c.c.	18	21	14	20	21	19½	
	3 c.c.	19	20	14	20	18	16½	After previous dose of digitalis

Upon grouping these experiments, I find: (1) Cases in which no slowing follows the injection (cf. 335, 334, 333, 361); (2) cases in which an immediate slowing takes place which is usually continued (cf. 339, 355, 360, 361); and (3) cases in which the slowing is late in its onset and sometimes preceded by an acceleration (cf. 333, 362).

To explain and harmonize these results and the effects of vagus section on them, I have formulated the following tentative hypothesis, which fits in with the data so far in hand but which future work may not substantiate. *The slowing of the heart occurring synchronously with the rise in pressure is due to a stimulation of the cardio-inhibitory centre. The slowing which is late in its onset is due to a direct action on the heart.* Either, both, or neither of these

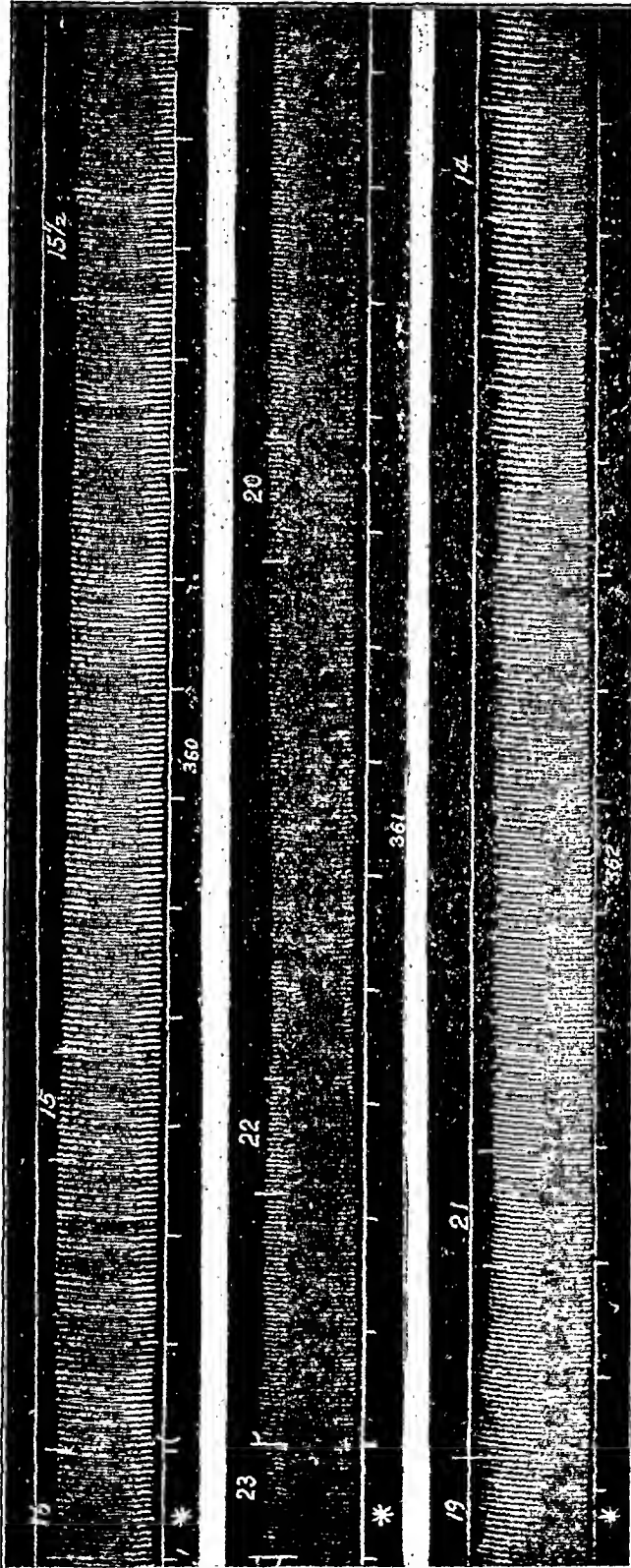


FIG. 2.—Three cardiographic tracings from different dogs, showing effect of 2 c.c. "pituitrin" injected at *. Upstroke, systole. Figures indicate heart rate per ten seconds. Upper curve shows temporary increase in amplitude followed by decrease, slight but immediate slowing (vagus action?). Middle curve shows an early decrease in amplitude, systole decreased, tonus increased. Slight early slowing (vagus action?), more pronounced later (direct cardiac action). Lower record shows a very temporary increase in amplitude followed by a decrease. Heart rate first accelerated, later markedly slowed (direct cardiac action?).

actions may follow the injection of pituitary extract, the factors determining the reaction being unknown. If both effects are present, vagus section will modify but not abolish the slowing. If the slowing is due to a vagus action alone, vagotomy will prevent the slowing, while, if late in its onset, and due to a depressing cardiac action, it will exert no influence.

It is quite generally assumed that pituitary extract increases the amplitude of contraction, an assumption which, in the majority of cases, it appears, is unfortunately based on no other evidence than the size of the oscillations of a blood pressure tracing which, of course, is no criterion of the strength of the beat. Oliver and Schäfer⁴¹ alone, so far as I have been able to discover, obtained myographic tracing of the heart. They concluded that these records showed an increase in the amplitude of contraction. Hebdom and Cleghorn⁴² obtained, on perfusing the apex of a dog's heart with extracts of the posterior portion of the pituitary gland, only a decreased amplitude of contraction, which was the rule in my own experiments. The tracings published by Osborn and Schäfer likewise show clearly that the augmentation of ventricular contraction is rather fleeting and followed by decrease in strength. With this discrepancy in mind, I carefully analyzed my own curves of the ventricular contraction recorded by a cardiograph, and in a few instances by a cardiac plethysmograph. The results of a number of these experiments I have also incorporated in Table II. They show that in 85 per cent. of experiments a decrease in amplitude of contraction, similar to that observed in the perfusion experiments, occurred. It took place synchronously with the late slowing in both cases. I therefore believe that pituitary extracts exert a late depressing action on the strength of beat as well as the rate of the heart. In a number of experiments, 20 per cent., this depression (which I consider the characteristic cardiac action) is preceded by a brief period of strengthened beat, sometimes accompanied by a slight acceleration and occasionally by a slight slowing.

THE DISSIMILARITY OF ADRENALIN AND PITUITARY EXTRACT. Both adrenalin and pituitary extract cause a rise in blood pressure, and for that reason the statement is often made in pharmacological literature that the two substances cause similar reactions. My results indicate that such a statement is not warranted. The likeness of the two reactions ceases with the rise in blood pressure, and, as regards its other actions, no two drugs could be more dissimilar. A comparison of the reaction of the two drugs may be made from the following summary:

⁴¹ Text-book of Physiology, i, 947.

⁴² Scand. Arch. f. Physiol., 1897, viii, 163; Amer. Jour. Physiol., 1899, ii, 273.

	Adrenalin	Pituitary Extract
Blood pressure	Rapid rise Temporary	More gradual rise Prolonged
Heart rate (Vagus intact) (Vagus cut)	Slowed chiefly by vagus action Accelerated Rarely slowed	Slowed chiefly by direct depressing action Slowed Rarely accelerated
Heart strength (Intact or perfused)	Increased systole Decreased tonus Amplitude increased	Decreased systole Increased tonus Amplitude decreased
Renal vessels	Constricts only Abolished by apocodein and ergotoxin	Constriction may be fol- lowed by dilatation Not affected by either

NUMBER OF ACTIVE SUBSTANCES IN PITUITARY EXTRACT. Since the pituitary extracts affect gland, nerve, and muscle cells as well as the heart and bloodvessels, and since no single chemical substance has been isolated, as is the case with adrenalin, it is not impossible that they contain more than a single active substance. The first suggestion that pituitary extract contains more than one chemically active substance was made by Schäfer and Vincent. These investigators pointed out that, although the first injection induced a rise in blood pressure, subsequent doses are less and less effective and may even cause a fall. Hence, they concluded that pituitary extract contained a pressor and depressor substance having opposite effects on the bloodvessels; that, in the case of the first injection, the pressor substance overpowered the depressor and, as tolerance developed, the latter substance alone remained active. At first, these investigators believed that they were able to extract the depressor principle with alcohol and ether, but in his most recent publication Schäfer explains this result as due to an imperfectly absolute alcohol. The depressing principle suggests cholin as far as its action on the blood pressure is concerned, but, according to Schäfer and Vincent, this substance acts on the heart, while they apparently attribute the action of the depressing pituitary substance to a dilator action on the bloodvessels. As we scan the curves reproduced by various workers, we many times obtain a suggestion of a fall in blood pressure, especially when more than a single dose has been administered. This may be attributed to a depressor principle, but unless accompanied by cardiographic records, such curves are difficult to interpret. In some cases, where I obtained a similar diminution, this fall was clearly due to a depression of the heart by pituitary extract, and not a vasodilation. At first thought the dual action on the perfused renal vessels might seem to supply evidence of two substances—a constrictor and a dilator. Even if subsequent experiments should indicate that a large percentage of perfused kidneys give such a reaction, this assumption need not be made, for, as I have shown before, a single chemical substance like

chloroform may cause such a double action. Furthermore, the constrictor reaction of the perfused kidney does not diminish on subsequent injection, much less is it supplanted by a dilation. Hence, further evidence is demanded before we can assume the existence of two principles affecting the peripheral vessels.

A second suspicion of two substances in pituitary extract was voiced by de Cyon, who believed he had isolated a substance (hypophysine) in alcoholic and ethereal extracts which acted to slow and augment cardiac contractions, while the residue extracted with water caused no cardiac effect but constricted the bloodvessels. Schäfer and Herring, however, on repeating similar experiments could not find any active substance in alcoholic extracts, nor could they find any difference in activity between saline extracts from fresh glands and from the residue left after previous extraction with alcohol and ether. Thus, the proof of separate substances acting on the heart and on the bloodvessels does not seem clearly established.

More recently, Schäfer and Herring came to the conclusion that pituitary extract contained a substance with a specific action on the renal cells. They based their contention on the fact that, although repeated doses of pituitary lose their pressure-raising ability, they retain their ability of promoting urinary secretion. Houghton and Merrill,⁴³ however, were not able to satisfy themselves that any diuresis occurred which could not be satisfactorily explained by the blood pressure changes.

Similarly, Pemberton and Sweet⁴⁴ believe that extracts of pituitary contain a substance capable of inhibiting the flow of pancreatic juice through action on the cells, but Edmunds⁴⁵ maintains that no inhibition occurs except as it is induced by changes in the blood supply. It is evident, then, that more convincing work will be necessary before we may safely assume the existence of more than one principle in extracts of the pituitary gland.

SUMMARY. In conclusion, it may be well to recapitulate briefly the chief ideas that I have sought to bring out in this paper.

1. Developmentally and histologically, the pituitary gland is composed of an anterior or epithelial portion and posterior or neuroglial portion.

2. The anterior lobe evidently elaborates a secretion that is necessary to life and to normal metabolism and development.

3. This substance has so far resisted extraction by various solvents, hence its chemical nature and physiological properties remain unknown.

4. The posterior lobe, which is not of vital importance, contains or secretes a substance that may be extracted by water, glycerine; or

⁴³ Jour. Amer. Med. Assoc., 1908, li, 1849.

⁴⁴ Arch. Int. Med., 1908, i, 634.

⁴⁵ Jour. Pharmacol. and Exp. Therapeut., Proc. of Society, 1909, i, 571.

salt solution, and resists boiling, but it has not been demonstrated that it is identical with the secretion of the anterior lobe or that it represents its vital principle.

5. These extracts constrict the peripheral vessels (probably by a direct muscular action), thus producing a marked rise of arterial blood pressure. This constriction is not equally pronounced in all organs, for the renal vessels are, at least passively, dilated during its action.

6. These extracts are generally stated to slow and strengthen the heart, but myographic tracings of the intact and perfused heart indicate a depressing influence to be the most constant and characteristic one, an increase in the amplitude being only exceptionally the case. The slowing, as well as depression, are largely attributable to a direct cardiac action, but the former may be augmented by a vagus effect.

7. Pituitary extract resembles adrenalin in its action only in that it causes a rise in blood pressure. The manner in which they affect the heart and bloodvessels, as well as the effects induced, are entirely different.

8. In addition to its cardiovascular actions, pituitary augments the secretion of urine and inhibits the flow of pancreatic juice, but it has not been definitely determined whether these varied reactions are due to separate substances, to a specific affinity of a single substance for different cells, or whether they are secondary to changes in the circulation.

STIFF AND PAINFUL SHOULDERS, WITH LOSS OF POWER IN THE UPPER EXTREMITY.¹

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Most physicians of experience have had patients with persistently stiff and painful shoulders and weakness of the arm, usually following some trauma to the shoulder, but sometimes without any history of such a cause, and they have been at a loss how to account for or to treat them. The complaints of the patients vary somewhat, but they are sufficiently similar to warrant the suspicion, at least, that most of them are due to a common cause, although some cases deviate from the usual type enough to raise the question of a common origin and to make the solution of the problem

¹ Read at a meeting of the Northwestern Medical Society of Philadelphia, September 5 1910.

a difficult one. It is very likely that the different stages in which the condition is met with by the physician, the varying nature of the injury causing it or the absence of any definite history of associated injury, the radiation of pain along one or more nerves or its localization in the region of the shoulder or at some other place, and the degree of atrophy present in the surrounding muscles have been responsible for the variety of terms under which conditions having probably a common pathological basis are diagnosticated. Many of them have been looked upon as rheumatic, and I believe that rheumatism can be responsible for it, although most of them are undoubtedly traumatic. Cases seen after dislocations or fractures about the shoulder, in which the limitation of movement is marked, have been called "fibrous ankyloses." It is very probable that the loss of power in the muscles, particularly in the deltoid, in large part due to the atrophy of disuse, has passed for a "paralysis of the deltoid." Undoubtedly many of those in which the pain radiates to the insertion of the deltoid, to the elbow or forearm, have been wrongly diagnosticated as cases of "neuritis." Often in such cases, if there is limitation of movement in the shoulder, it is slight and not easily recognized on account of the associated movement of the scapula. In one case a prominent surgeon made the diagnosis of traumatic arthritis, on account of the prolonged pain and stiffness in the shoulder. This patient, while riding in a street car with his well arm carrying parcels, managed to raise the hand of the affected side high enough to catch a strap with which to steady himself. The car suddenly gave a lurch, unbalancing the patient in such a way that the strap hand was compelled to support his whole weight. There was a sudden snap in the shoulder, with severe pain, but from that moment, the patient says, the stiffness of the shoulder disappeared and some time later the pain, so that gradually the shoulder returned to its normal condition. It is very unlikely that such an accident would have cured a traumatic arthritis.

The one feature that characterizes the cases which I have chosen for discussion is a more or less marked limitation of abduction and rotation in the shoulder-joint, never complete but usually crippling and very persistent. In the early stages there is always acute pain about the joint, often radiating to the arm, sometimes to the forearm, or even to the hand. There is loss of power in the muscles of the shoulder and arm not readily accounted for entirely by the pain on motion. Indeed, in the later stages there may be little or no pain, although even then there will usually be pain if the restricted motion is forced. When the pain in the shoulder has disappeared, it is frequently found to radiate down the arm, often about the insertion of the deltoid. Scapulohumeral limitation of movement is always present in some degree. Jarjavay, in 1867, and Duplay, in 1872, accounted for the condition by

assuming the existence of a periarthrititis, which localized itself particularly in the subdeltoid or subacromial bursa. More recently Küster,² in Germany, and Codman,³ in this country, have again called attention to the importance of an inflammation of this bursa in the causation of these stiff and painful shoulders.

Codman's work has received wide attention in this country, and it may be said that his conclusions have been generally accepted. For some time I have entertained a conception of the pathology of these cases, which differs decidedly from that based upon the bursitis theory, and so far as I am aware it has never been offered before. I believe that we have to do with a periarthrititis in these cases, but not of bursal origin. Whoever would hope to attract any attention to a new theory must recognize the fact that no other has seemed to account so well for the wide variety of symptoms and associated conditions, as that based upon an inflammation of the subdeltoid or subacromial bursa. In my opinion, Codman's paper is the strongest we have on the subject, in that it presents positive evidence of firm bursal adhesions in a considerable number of cases operated on and cadaver specimens. In one cadaver specimen, with the typical limitation of movement, even after the division of all the muscles of the shoulder and the anterior part of the capsule, the subdeltoid adhesions alone maintained the limitation of abduction and external rotation. Yet, notwithstanding the evidence produced by Codman, there is still room for discussion as to the pathology of this condition, and I am disposed to regard the bursitis theory as not proved. The one cadaver specimen, in which it was demonstrated clearly that the subdeltoid adhesions were responsible for the scapulohumeral ankylosis, merely indicated, I believe, that there had been an unusual inflammation in the bursa in this case. As for the others, the cadaver cases and those operated on, I do not believe that the fibrous bands found account for the resistance to the force which is necessary to overcome the limitation of motion. There are other reasons why they probably do not, but I wish to call attention here to one objection to this theory, drawn from Codman's paper. He says: "In some of these cases which are etherized and manipulated the adhesions may be felt to tear, sometimes with alarming violence, so that one suspects fracture of the humerus or rupture of the internal lateral ligament of the elbow." In one of my cases I thought that I had surely torn some ligament at the elbow, and in another the same sensation was observed to a milder degree. In this second case there developed in a few days a distinctly localized area of ecchymosis over the internal condyle, indicating that something had been torn there. Codman believes that the tearing

² Archiv f. klin. Chir., 1902, lxxvii, 1013.

³ Boston Med. and Surg. Jour., 1906, cliv, 613.

at the shoulder occurs in the subdeltoid and subcoracoid bursæ, possibly also in the older cases in the substance of the contracted and shortened subscapularis muscle, and that the tearing sensation over the internal condyle occurs simultaneously with and is due to the tearing at the shoulder. He says, further: "In six cases I have made an incision into the bursa on the point of the shoulder between the fibers of the deltoid, and have torn the adhesions with my fingers *before using the leverage with the arm*. In two cases it was necessary to divide the adhesions with scissors." He clearly implies that it is the leverage with the arm that produces the alarming tear, which suggested the rupturing of the internal lateral ligament of the elbow, even after the adhesions in the bursa have been thoroughly broken by the fingers or divided by scissors. Where is the resistance that calls for such force after the subdeltoid adhesions have been removed? Surely not, as suggested by Codman, in the small, delicate subcoracoid bursa, which is sometimes absent. If the shoulder can perform its normal function without this bursa, then adhesions in it will not interfere much with its movement.

I have dissected this bursa eight times, four times after injecting it with plaster of Paris. Except the subscapular, it is the largest of the bursæ about the shoulder, of which some anatomists enumerate as many as ten. I cannot agree with Codman and Küster in regarding it as a very extensive and complicated serous sac. Küster says that it extends above deeply under the acromion, below over the greater part of the anterior joint region, between the deltoid muscle and the joint capsule, and externally reaches as far as the greater tuberosity. I observed that in every one of my specimens, except one, it was circumscribed to the upper surface of the greater tuberosity (Fig. 1), and to a small portion of the supra- and infraspinatus tendons inserting into the tuberosity. In one specimen it extended somewhat farther inward toward the coracoid process (Fig. 2). When the arm is at the side of the body and the forearm across the front of the chest, the greater tuberosity lies in front of the acromion process, the bursa then being covered by the corresponding portion of the deltoid, the fibers of which are here very thin and the greater tuberosity easily palpable under it. Only a small part of the bursa extends under the acromion, about a half inch (Fig. 2). It is very simply constructed, with regularly defined borders, and it is slightly elongated antero-posteriorly. It has a diameter of approximately two or two and one-half inches. With the overlying deltoid removed, as the head of the humerus is rotated externally, the bursa is seen to move with it because it is firmly adherent to the tuberosity, and as it moves gradually changes its shape, becoming smaller. In full external rotation, the subdeltoid portion, *i. e.*, the portion exposed beyond the edge of the acromion, is very much smaller than in internal rotation (Fig. 3). The subdeltoid portion is now external

to the acromion, and if the arm is abducted to an angle of 45 degrees it becomes almost entirely subacromial. It always follows the



FIG. 1.—Front view. Bursæ injected with plaster-of-Paris. Both arms in sling position (adduction and internal rotation), except for slight abduction in right. Both bursæ anterior to acromion and extending about one-half inch under it. Right about normal size, left about one-third larger from forced injection. □



FIG. 2.—Lateral view from above. Bursa overdistended from forced injection. Effect of the exposure to camera is to make bursa appear relatively larger than in actual specimen. It is, however, wider than in any other of the eight specimens examined. It extends under the whole length of the coraco-acromial ligament to the coracoid process. It is probably continuous with the subcoracoid bursa. The extent of the subacromial portion in this position of the arm is fairly well indicated.

greater tuberosity, which is now under the acromion almost entirely (Fig. 4). It is evident that its attachment to the overlying deltoid must be very loose to permit so great movement of the bursa under the muscle, and so great a change in its shape. The wall of the



FIG. 3.—Right arm of specimen shown in Fig. 1, is in full external rotation. The bursa carried by the greater tuberosity to which it is attached, is now external to the acromion and is slightly diminished in size.



FIG. 4.—Same specimen as in Figs. 1 and 3. Right arm in full external rotation and abducted to an angle of about forty-five degrees. Bursa almost entirely under acromion.

bursa is exceedingly thin, of tissue paper thinness. There must be a very decided change in its thickness and in the firmness of its attachment to the overlying deltoid before it can offer the resistance to movement which is found in the cases under discussion.

The resistance from bursal adhesions can be no stronger than the bursal walls.

The position of rest in the shoulder after an injury, or when the joint is inflamed, is with the arm in adduction and internal rotation. The limitation of movement is from this position, *i. e.*, into abduction and external rotation. With the arm in the position of rest, the bursa is almost entirely subdeltoid and directly in front of the acromion, over the greater tuberosity and under the thin portion of the deltoid, where the tuberosity is easily palpable. It is evident that if the bursal adhesions are to limit the movement of the humerus, the normally loose upper bursal wall must have become firmly fixed to the overlying deltoid by new and dense cicatricial or inflammatory tissue. Under such circumstances, if there were any movement of the greater tuberosity it could only be by dragging with it the adherent deltoid, which is here so thin that movement of it could easily be recognized by its effect on the overlying fascia and skin. I have been convinced in my cases that the movement of the tuberosity was distinctly under the deltoid and about as independent of it as in a normal shoulder.

Codman says that in the acute stages of a bursitis about 10 per cent. of painless motion is possible in the shoulder without calling into play the inflamed surfaces of the bursa. According to my observations, the floor of the bursa follows the greater tuberosity in its slightest movements, and that means that any movement of the arm, and therefore of the shoulder, brings the opposed inflamed surfaces into play. Küster makes similar statements, and goes so far as to say that even a push on the upper arm against the glenoid cavity does not give the slightest pain. I should say that if such a test did not elicit pain, there was no inflammation in the subdeltoid bursa, surely not acute enough to produce troublesome adhesions later. Again, Codman says that the local tenderness is sometimes definite enough to allow accurate mapping out of the bursa, especially in cases of inflammatory origin involving the whole bursa. It is difficult to conceive of an inflammation in a serous sac of the size of this bursa, intense enough to produce troublesome adhesions later, which does not involve the whole bursa. I doubt that such a bursitis could remain partial. I have seen, repeatedly, acute inflammation in other bursæ, as the prepatellar, that over the olecranon, and the "bunion" bursa, but there is rarely any doubt as to the diagnosis in them. Even if there were no redness or swelling, the acute tenderness would be so distinctly localized and so marked that no other condition would be suggested. I believe that the tenderness should be just as acute and as easily localized in a subdeltoid bursitis, especially when the arm is in the position of rest. The bursa, as already stated, is then almost entirely under the muscle and directly in front of the acromion. The tuberosity upon which the bursa lies

is almost subcutaneous, so that by pressure with the finger downward on the bursa against the bone, exquisite tenderness should be elicited and the limits of the bursa outlined almost exactly. The absence of tenderness should positively exclude bursitis. A push on the upper arm against the glenoid cavity would drive the upper end of the humerus against the under surface of the acromion, and, therefore, the inflamed surfaces against each other. Rather than not give the least pain, as Küster states, it should give acute pain, and the fact that it did not give pain in Küster's cases tends to show that the real trouble was elsewhere. The symptomatology of these cases in their various stages, as outlined by Codman and Küster, is essentially the same, and agrees with what I have observed in my own cases.

The etiology offered by both these writers is not satisfying, in my opinion. The relationship shown between cause and effect is not convincing. Codman suggests a variety of causes under the general headings of trauma, fixation of the arm and shoulder by dressings, and infections. Infections of this bursa are admitted to be very rare, and they will not be discussed here, since the cases under discussion are distinctly traumatic, or at least not pyogenic. Under trauma are suggested a direct blow from a fall, sudden muscular exertion, pressure as from a misapplied bandage, overuse as in a base-ball pitcher, and unaccustomed exertion without proper previous training. I believe that in a fall there is small chance for a direct blow on the bursa, which is on the top of the humerus, and with the arm at the side, is in front of the acromion. Indeed, I believe that a conscious person in falling practically never keeps his arm at the side of the body, but that he will from the instinct of self preservation unconsciously break the force of his fall by putting out the arm rigidly extended at the elbow and striking the ground with the hand. Such use of the limb accounts, I believe, for the great variety and frequency of injuries to the upper extremity and makes unlikely frequent striking on the shoulder. The falling of the arm to the side of the body before the patient realizes what has happened and the severe pain in the shoulder will account for the statement of the patient that he struck on his shoulder. Direct blows are not frequently productive of acute inflammation in the more exposed bursæ, and inflammation should, therefore, be much less common here. The function of the bursa is to provide for sudden muscular exertion and to obviate its untoward influence. It rarely produces inflammation in other bursæ. Again, misapplied bandages, overuse, and unaccustomed use are unlikely causes of inflammation here. Most bandages applied to the shoulder are used to immobilize the arm at the side of the body, and in my experience they usually tend to slide upward and rarely make firm pressure over the upper end of the humerus. Bandages about the elbow and knee are more likely to produce bursitis from

pressure, but very rarely do so. Nor do I believe that long fixation, as in the treatment of fractures, will cause a bursitis. Fractures of the upper end of the humerus or dislocations may injure the bursa, but rest alone can scarcely be regarded as a cause of inflammation in it. In my opinion neither the symptomatology nor the etiology as given by Codman and Küster localize the seat of the trouble in the subdeltoid bursa.

I have seen in all 14 cases of these stiff and painful shoulders. They varied more or less from each other, but the differences were of degree rather than of kind. The scapulohumeral ankylosis, the pain particularly upon forced movement, and the impaired power of the muscles of the extremity, especially of the arm, were present in all. In all but 3 a clear history of trauma was obtained, and in 2 of these trauma could be excluded. In the other there was a vague history of muscular strains on several occasions, but I am now inclined to believe that it was not traumatic, but rheumatic. In 4 cases there had been a dislocation of the ordinary anterior variety in each. It seemed easy enough to account for the condition when it followed a dislocation, but in those in which there had been no dislocation the pathology did not apply. Yet I felt satisfied that it was essentially the same in all. The cadaver specimens in the department of Applied Anatomy of the University of Pennsylvania, through Dr. G. G. Davis' kindness, were always at my service, and I consulted them frequently. After reviewing the mechanism of the dislocation, with the aid of the dissected dislocation specimens and those in which the joint was unopened, it occurred to me that a sprain of the shoulder from forced abduction might explain those stiff and painful shoulders not due to dislocations. The difference between a sprain and a dislocation is often a narrow one. A sprain is the result of indirect violence which forces a movement of a joint beyond its physiological limits, with a stretching or tearing of the strained ligament. I believe that ligaments do not stretch much, but usually tear under these circumstances. There may even be a temporary dislocation with immediate reduction.

We hear very little of sprains of the shoulder, and yet when a force is applied to it sufficient to carry it beyond its physiological limits, something must give way. From my study of the joint specimens, I have satisfied myself that it is the capsule which makes the last stand for the protection of the integrity of the joint. In producing a dislocation of the shoulder on the cadaver by forced abduction, the first sensation of a giving way in the joint is synchronous with an audible tearing. On dissecting the specimen after the dislocation, usually nothing else will be found torn except the anterior and lower part of the capsule. The fact that the capsule tears extensively every time and usually alone proves that it is the structure which feels the first strain in overabduction of the

shoulder. Now, when we study the shoulder, we find that movement cannot be carried beyond the normal in adduction, the body being in the way. Therefore, the upper part of the capsule cannot easily be torn by such a movement. Movement of the arm forward and backward as in the pendulum movements, merely twists the capsule in its whole circumference, so that a tear is much less likely than if the strain were put on any one part of the capsule. To put the posterior portion of the capsule on a strain the arm must be carried forward and inward across the front of the chest, which again obstructs the movement. The portion of capsule most frequently and most violently exposed to strain by movement of the arm is the lower and anterior part, from forced abduction. From the position of rest at the side of the body, this is the least restricted movement of the arm, and when the force is applied to the hand with the elbow in extension, as in a fall on the hand, we have a very powerful leverage action at the shoulder.

The long axis of the glenoid cavity is directed from above downward and backward, so that the portion of the capsule usually regarded as anterior, that is, the portion anterior to the attachments of the long head of the biceps to the upper margin of the glenoid process and the long head of the triceps to the lower margin, is in reality the antero-inferior portion. What is probably not generally appreciated is that the axillary portion of the capsule is almost entirely anterior to the glenoid cavity as we determine its boundaries. When the arms are raised in abduction, we can see the whole axilla from in front, while it cannot be seen at all from behind. The effect of forced abduction, therefore, is to strain the axillary portion of the capsule. If the force is sufficient, this portion is torn more or less extensively. If greater force is applied, and particularly if a thrust is added, as in a fall on the hand, the humeral head is carried over the anterior glenoid margin and we have a dislocation. The freedom of movement in abduction, unhindered except by the axillary portion of the capsule, and the frequency with which it is forced beyond its physiological limits, account, I believe, for the overwhelming preponderance of anterior dislocations. Forced abduction is the accepted cause for most dislocations of the shoulder, and this cause can only produce an anterior dislocation. As soon as the patient assumes the upright position the arm falls to the side of the body and the humeral head rises to a position just under the coracoid process. Rarely the head may catch in the axillary tissues so that the arm cannot fall from gravity, when we have a *luxatio erecta*, which occurred in one of my patients who developed a scapulohumeral ankylosis, or the head may rise part way and catch in a somewhat higher position, when the arm falls only to about the horizontal position, and we have a *luxatio horizontalis*.

Undoubtedly in many cases, as the arm falls the head fails to

catch in front of the glenoid process, and a spontaneous reduction is the result. It has frequently been my experience in cadaver work to find that after the capsule has been felt to tear, considerable force was still necessary to effect the dislocation. Sometimes after the dislocation is produced still more forcible manipulation is necessary before the dislocated position can be maintained, when the arm is brought to the side of the body. The obvious inference from these facts is that many times in the living not enough force has been applied to produce a dislocation that will persist after the arm falls to the side of the body, and probably much more often the capsule is torn in various degrees short of that which is necessary for the occurrence of a dislocation.

Let us assume for the present that the forced abduction is the result of a fall. At the moment of impact the patient is so distracted that he is not capable of observing and afterward of recalling what was the actual position of the arm at the time. Most patients are not made unconscious from such an accident, and immediately afterward sit up or stand. In the meantime the arm may have been in various positions before it fell to the side of the body, and the patient is not impressed with the importance of any one of them. What he does know is that he fell and has pain in his shoulder. The simplest explanation to him is that he struck on the shoulder. A case seen with Dr. J. W. McConnell was very suggestive in this connection. The patient was descending a vertical ladder, when his feet slipped. The weight of his body compelled first one hand to lose its grip and then the other, and he fell to the ground. The patient accounted for his stiff and painful shoulder, which was accompanied by loss of power in the arm, by saying that he struck the shoulder on the ground. It was the shoulder on the side of the hand which was the last to lose its grip that became stiff and painful, and that was the shoulder probably exposed to the most severe abduction, as it was with that hand that he had the last chance to save himself from falling. The results of treatment, so far as they can, confirm the diagnosis of a contracted capsule. Dr. McConnell had had a fairly large experience with similar cases, and had hitherto treated them on a basis of a traumatic neuritis, with electricity, massage, and passive motion. In this case, in addition to the other measures, he employed forced abduction, to stretch a supposedly contracted capsule, and had the patient apply this exercise whenever possible, as by hanging from a horizontal bar or by any other means that presented itself. Recovery was very much more rapid than in any case he had previously treated.

A tear of the axillary portion of the capsule may occur in the absence of a fall or severe violence of any kind. I have seen a case in which there was one of these stiff and painful shoulders, of about eleven weeks duration, which was diagnosticated as a

circumflex neuritis, chiefly because the woman after careful questioning could not recall having sustained any injury to the shoulder. The *x*-rays showed a complete subcoracoid dislocation of the shoulder, which in my opinion implies an extensive tear of the capsule. She then recalled that about the time of the beginning of her trouble she had tried to move some heavy furniture, and had done something else of the kind, but she could not say which, if either, had started the disturbances in the shoulder. Another patient dislocated her shoulder while raising her arms above her head in the act of "stretching," when the rocking chair in which she was sitting tipped backward suddenly. There was considerable pain in the shoulder afterward, but not enough to prevent her from going to the theatre the same evening or to cause her to call her physician, although her husband was a dentist whose intelligence and solicitation would have led him to call a physician if there had been any suspicion of a dislocation. If the capsule will tear sufficiently to permit a complete dislocation without more evidence of it than developed in these cases, then it may be assumed that less severe tears from overabduction and muscular action are common and are not detected.

Codman cites, as a cause of subacromial bursitis, the vigorous friction produced between the bursal surfaces by a baseball pitcher in violently throwing a ball. May not the trouble which follows be due to a tear of the capsule? A dislocation of the shoulder has been produced by this action. The movement here is first into extreme abduction, from which position the hand and arm are brought downward and forward with much force, by the powerful adductors forming the folds of the axilla and having their insertions into the upper end of the humerus. With the axillary portion of the capsule under tension, the powerful pull of these muscles against it might readily tear it. A similar tear might be the result of getting off a street car with the hand gripping the hand rail and the body being dragged by the arm, if the patient lost his balance. I have already referred to a patient who probably received his injury from suddenly being compelled to support his whole weight on one hand with the arm in full abduction. It is unnecessary to go further in suggesting how in common accidents a tear of the capsule from forced abduction could occur.

Sprains in most joints are recognized easily, why not in the shoulder? Because the arm usually drops to the side of the body before the patient recovers from the excitement of the accident. The importance of the indirect violence which produced the forced abduction, is lost sight of, and the more obvious direct violence from the fall attracts attention. The seat of the lesion in the capsule is so deeply situated in the axilla that it cannot be localized by the symptoms which follow. The arm is kept at rest by the pain, that is, with the elbow at the side and the forearm across the front

of the chest. Abduction and external rotation pull upon the torn portion, adduction and internal rotation relax it. Since the nature of the lesion is not suspected by the attending physician, he advises rest in the most comfortable position, and too often it is kept in this position until the tear has healed and the capsule firmly contracted in its relaxed portion. The more severe the tear the greater the amount of inflammatory material formed about it and the more rigid the contraction. The blood and lymph from the torn vessels and the synovial fluid from the joint, freely opened in the dependent portion, extravasate around the muscles, the blood-vessels, and the nerves, and aggravate the rigidity of the joint. The nerves become involved in the inflammatory process which ensues, and later are bound down by the cicatricial tissue and adhesions. The pain is most marked in the early stages in the region of the lesion, but later may be transferred along the course of the imprisoned nerves. It is not material to account for the exact location of the transferred pain. I have seen it referred to the wrist. It is my belief that serious rupture of the nerves, even of the circumflex in dislocations, is comparatively rare, and that the prognosis with proper treatment is very good in the great majority of cases.

If the importance of the causal movement is not appreciated, it may be forgotten by the patient and a traumatic history may not be obtained, as in the case already referred to, in which a diagnosis of circumflex neuritis was made and a dislocation found later. A case ascribed to rheumatism may have originated in a forgotten injury, but it may be due to rheumatism. I have seen a case in which both shoulders were involved and rheumatism was partly at fault. This patient was a young lady who had been acting for several years as her father's secretary. About three weeks after the trouble began in her shoulders and in other joints, she fell down two steps, but did not observe that the accident was followed by any decided increase of the pain in the right shoulder. Yet it was this shoulder which gave her most trouble. Her physician, on account of the marked weakness in her arm and hand, and her inability to write, diagnosticated a writer's cramp. Upon consulting a second physician, he called it a neuritis of the arm. About six weeks after the fall, a third physician said that he discovered a dislocation of the shoulder, which he reduced without an anesthetic. Both the patient and her father are certain that there had existed, before the reduction, a depression below the acromion into which the fingers could be pushed. This symptom alone, in my opinion, justifies the diagnosis of a dislocation, particularly as the depression below the acromion disappeared after the reduction, which was followed by immediate and marked improvement in the shoulder and arm.

In a second case the condition could not have been due to trauma,

but was due to a non-traumatic inflammation of both shoulders. This second case was examined by a neurologist, who diagnosed a chronic anterior poliomyelitis. The prompt improvement under massage and passive movements eliminated the spinal cord condition. If the arms are maintained in the position of rest during a prolonged attack of rheumatic inflammation, it is easily conceivable that the capsule should become more or less thickened and rigid, the axillary portion becoming shortened because relaxed. After the subsidence of the attack, when an attempt is made to abduct the arm and rotate it externally, the contracted axillary portion will offer resistance according to its degree of rigidity. The great majority of the cases, however, are distinctly traumatic.

Upon the basis of a torn capsule, I believe that all the various symptoms peculiar to these cases can be explained. The scapulo-humeral ankylosis will vary widely, but is never complete, because there is always some remaining laxity in the affected portion of the capsule. If a severe tear of the capsule occurs in an old woman who has nothing else to do but nurse it, and particularly if she is very sensitive to pain, an aggravated case will result. One of the worst cases I have seen was in an old woman, who from a fall had sustained a fracture of the neck of the femur, which compelled her to lie in bed for many weeks. She had complained of pain about the shoulder after the accident, and some ecchymosis had appeared, but the x-rays did not reveal a fracture, and nothing was done for the shoulder except to keep it at rest. The limitation of movement in the shoulder and the atrophy of the surrounding muscles were very marked when I first saw the patient, about ten weeks after the accident. If the capsule tear is a slight one in a strong, active, and ambitious man, who persists in forcing the use of the arm at every opportunity, the return of function will be much more rapid, although even in such a case many weeks may be necessary before the normal range of motion is obtained. It is in the later stages of the latter type that the scapulo-humeral ankylosis may be most difficult to detect, and for that reason the diagnosis may be very uncertain. The loss of power in the arm may be very marked, or there may be a very troublesome pain radiating down the arm. I have thought that the inclusion of the nerves in the old area of inflammation must be largely responsible for both. I have seen one case in which there was a slight scapulo-humeral ankylosis, detected only by careful watching of the scapula and comparing its movement with the opposite side. Yet there was a marked weakness of the muscles on that side, although they seemed to be almost as well developed and to contract almost as well as in the normal arm. In another case, in which the ankylosis was marked and of long standing, there was considerable loss of power in the arm, but I had not paid particular attention to the condition of the hand. Under ether I forced the arm into

full abduction and fixed it there. He had not recovered from the anesthesia when I left him, and on the following day he expressed much satisfaction because he could, since he became conscious, perform all the normal movements of the hand. He said that before taking the anesthetic, the hand movements were much impaired and weak, but soon after recovering from the ether he found that they had all returned as if by magic. It would seem, therefore, that the limitation of movement in the shoulder *per se*, was responsible for some of the loss of power. On the other hand, almost the full power of the muscles may apparently return in time, though the limitation of movement persist. I have seen a patient with scapulohumeral ankylosis of about twenty-five or thirty years duration, so marked that the arm could be abducted only to a right angle with the body, and that with the associated movement of the scapula, yet there was only slight loss of power in all the muscles employed in producing the limited movements.

The following case is the best example in my experience, illustrating how a diagnosis of neuritis is made in some of these cases. I was visiting the patient as a friend, when he informed me that he had been under the care of his family physician for some time for a "neuritis" of the arm. The patient and his physician believed that the most likely cause was a habit of sleeping with his head resting on the arm. The pain was most marked at about the insertion of the deltoid, but radiated down the arm to the elbow and into the forearm. I was asked to examine the arm and did so, but I did not make a diagnosis. On another visit I found that he had tried various treatments, including "electrical treatment" and a patent medicine. The condition was still regarded as a "neuritis," and no one had ever suggested the possibility that anything might be wrong with his shoulder. Having become interested in these stiff and painful shoulders by this time, I tried the shoulder in this case and found a very marked limitation of abduction and external rotation and some slight grating on movement. I had not yet satisfied myself concerning the nature of these cases, and I thought that I was dealing with a case of osteoarthritis, and had his physician send him to a well-known orthopedic surgeon, who concluded that it was a case of osteoarthritis. Later the patient fell into the hands of an osteopath, who among other treatments carried out a vigorous series of forced exercises calculated to increase the limited movements, and after a prolonged period gave the patient a practically normal arm and shoulder. He did not have "neuritis," nor did he have osteoarthritis. He probably had had some time previous to the pain in his arm an attack of inflammation from rheumatism or an overlooked trauma in the shoulder, which had brought about a contraction of the axillary portion of the capsule, which in turn was lengthened again to the normal by the forced abduction and external rotation.

The most convincing evidence, in my experience, that these stiff and painful shoulders are due to a contracted capsule, is the fact that identically the same condition, so far as I can see, is present after the operation of contracting the axillary portion of the capsule for a recurrent dislocation of the shoulder. I have done this operation in eight cases, and I can see no essential difference between the two classes of cases, except in the results of the efforts to obtain movement. After the operation I can get movement in the shoulder more quickly and with less pain than in a case in which the capsule has recently been torn by accident. It may be that in the latter the extravasation of blood and synovial fluid among the axillary tissues produces a greater degree of inflammation and rigidity than follows the operative trauma. I had one experience in which I was positively convinced that the stiff and painful shoulder, in this case at least, was due to a contracted axillary portion of the capsule, because in that one the tearing sound produced by the leverage of the arm when it was forced into full abduction under ether, was accompanied immediately by a dislocation of the humeral head into the axilla. In my opinion, a traumatic dislocation of the shoulder implies an extensive tear of the capsule.

TREATMENT. While there seems to be a tendency to slow improvement in the function of the shoulder from long-continued efforts to use it even when untreated, I have no doubt that many cases remain seriously crippled through life. I know of one case in which the arm, after a dislocation of the shoulder about four years ago, is still seriously limited in the range and power of its movements. I have already referred to a case in which there is still marked limitation of movement, although the power is good and there is no pain twenty-five to thirty years after the original accident. A medical friend informed me that his grandfather died at a ripe old age, still carrying one of these stiff shoulders which was the result of an accident in early life. I believe, however, that with persistent treatment based upon the pathology which I have offered, practically all of them can be given normal, or nearly normal, function. In some there may be serious nerve lesions, but these are probably far from frequent. The majority of these patients will likely call for the physician's aid sometime after the original accident, when the limitation of movement and pain threaten to become permanent. If they are seen early and are very painful, the most important indication will be to provide rest of the shoulder by immobilization. During the early stages it may be necessary to immobilize it for a week or two, but during this period, at each change of the dressing, massage and passive movement within the painful limits is advisable.

The position in which the arm is to be immobilized is of importance. Küster applies a plaster cast with the arm at the side of the body for eight to fourteen days, and then begins careful passive movements, baths, and massage. Codman prefers to keep the

arm in abduction to a right angle or more. I regard this as a distinct advantage in reducing the later limitation of motion. I should prefer to vary the position in this stage according to the type of patient. If I were treating an ambitious young man who insisted upon attending to his business, I would dispense early with the fixed abduction, bind the arm at the side, and support the wrist in a sling from the neck. I would remove the dressing daily, and as soon as the pain would permit begin gentle massage and passive movements, gradually increasing the force until the length of the injured portion of the capsule and therefore the motion had been increased to the normal. If the patient were a highly nervous and sensitive woman, I would advise her to remain in bed, and would then adopt some measure for keeping the arm in full or nearly full abduction. This would permit healing of the injured portion of the capsule at nearly its normal length. If an obtuse angled splint is employed, this may be removed daily, when gentle massage and passive movements could be carried out. At the end of two weeks, or at most three, the arm may be lowered to the side of the body gradually, after which it can be brought back to the fully abducted position more easily than if it had been dressed at the side in the early stages. If the patient will not remain in bed, and, in the case of a man, if he is content to remain away from his business for a week or two, it becomes necessary to find a method of fixation of the arm in the abducted position that will permit him to walk about. This is not as simple a matter as at first it might seem. The position is an awkward one, exposes the patient to considerable discomfort, and the splint and bandage to such a strain that they tend to become disarranged. Monk's splint with Codman's modification is a particularly good one. In a case of subacromial dislocation in a boy upon which I operated, and in which I wished to maintain the fully abducted position for two weeks, I employed a light palster cast encircling the chest and the arm to but not including the elbow, and found it very satisfactory.

After the reduction of a dislocation of the shoulder we have the same problem to deal with, although the statistics of Schulz⁴ show that we do not appreciate the fact. In these cases, however, the capsule has been so extensively torn that if we dress the arm in the fully abducted position we are in danger of permitting a recurrence and of the development of a recurrent dislocation. In Schulz's 54 dislocations of the shoulder, in not one was a recurrent dislocation developed. It would seem that the treatment was at fault in the opposite direction, that is, not enough force was employed in overcoming the cicatricial contraction of the torn axillary portion of the capsule in the early stages. At the end

⁴ Deut. zeit. f. Chir., 1908, ix, 333.

of three weeks of rest of the arm at the side of the body, abduction with moderate force should be begun, and at the end of five or six weeks I believe that there will be little danger of producing a recurrence of the dislocation.

If the case comes under observation in the late stages, after the cicatricial tissue in and about the torn capsule is firmly contracted and very resistant, the effects of forced abduction may be so slight, and the return of motion so slow, that it becomes advisable to anesthetize the patient and to break the resistance completely at one sitting. The scapula should be immobilized with one hand, while with the other grasping the elbow the humerus is used as a lever to tear the shortened capsule. The tearing at the shoulder may be felt or even heard. Sometimes a tearing sensation is felt over the internal condyle at the elbow. Codman believes that this sensation at the shoulder is due to the giving way of adhesions in the subdeltoid and subcoracoid bursæ. The sensation at the elbow, he thinks, is due to the transmitted vibration along the coracobrachialis muscle to the centre of the humerus. I believe that the tearing at the shoulder is of the contracted axillary portion of capsule, and in one case, which has already been referred to, I was sure of it because immediately after the tearing sensation occurred I found that I had to deal with an axillary dislocation of the humeral head. I maintained nearly full abduction on a splint for about ten days, before letting the arm down to the side of the body. After about four months the patient had not had another dislocation and had nearly full motion at the shoulder. Nor do I believe that the sensation at the elbow is a transmitted one, because a few days after the forcible manipulations in one case, in which I felt the tearing sensation over the internal condyle, there appeared a slight but distinct area of ecchymosis over the internal condyle, showing that something had actually torn there. I prefer to believe that the slight injury at the elbow was due to the pull on the triceps, the long head of which is caught in the contracted cicatricial portion of the capsule.

After the capsule has been torn and full abduction produced, provision must be made for maintaining that position, just as in some cases in the acute stage following the original accident. After using force to break the resistance, Küster dresses the arm for a time at the side of the body, and he speaks of the necessity of frequent repetition of the "breaking of adhesions." He says that only in very old cases should the hope of complete success be abandoned. I have had four cases in which I used force under the influence of an anesthetic, and in none was it necessary to repeat it. In one, a young, vigorous man, there was perfect function in three months, and in another, also a young man, there was almost full motion in the shoulder in six weeks, when I lost sight of him. In the two others, one a man and the other a woman, both

about sixty-five years of age, there was nearly full function in four months. One is still under treatment and the other had nearly full function when she disappeared.

The principle is the same as when the tendo-Achilles is divided for talipes equinus. As the gap in the tendon is bridged across, so the gap in the torn capsule, which is probably not more than a half inch wide, is filled in with new cicatricial capsule in a short time. After two weeks rest in the abducted position, the arm is gradually lowered to the side of the chest. Massage and passive motion are then depended on to bring about a return of function in the joint and atrophied muscles and a stretching of the adhesions and absorption of the inflammatory material about the nerves and vessels in the axilla.

In those cases in which the scapulohumeral limitation of movement is slight and the pain referred down the arm marked, the question arises as to whether forcible abduction is advisable to tear the slightly shortened capsule. In the one case of this kind in which I tore the capsule, the patient as soon as he recovered from the nitrous oxide anesthesia, said that he had felt the tearing at the shoulder, and expressed the belief that the real cause of his trouble had been removed. After a few days rest in bed, with the arm in full abduction on a splint, I allowed him to get out of bed with the arm at the side, but only on the promise that he would permit full abduction at least once daily. The marked lack of power and the severe pain in the arm, particularly on efforts to abduct it, which had persisted for eight months, during which time he could not follow his usual occupation as a machinist, rapidly improved, so that in six weeks after the forcible manipulations he was able to return to work at his trade. This is the best kind of evidence that the slightly contracted capsule, was chiefly responsible for the "paralysis" and the pain which had been ascribed to a "neuritis."

CONCLUSIONS: A periarthrititis from tears of the axillary portion of the shoulder capsule, due to forced abduction, offers the best explanation of the stiff and painful shoulders, with loss of power in the arm, variously diagnosticated as fibrous ankylosis, neuritis, paralysis of the deltoid, traumatic arthritis, etc.

The most characteristic feature is a scapulohumeral limitation of movement, sometimes slight, often marked, but never complete. The associated loss of power and atrophy are due in part to disuse, but probably in most part to the perineuritis, neuritis, and resulting adhesions and compression of some or all of the brachial nerves in the axilla, adjacent to the wounded joint.

Subacromial, or subdeltoid bursitis does not explain satisfactorily the symptomatology in these cases, nor is it accounted for by the etiology usually suggested. The audible and palpable tearing which accompanies the breaking up of the limited abduction and

external rotation, in chronic cases, by the leverage of the arm, under an anesthetic, is produced not by the tearing of fibrous adhesions in the bursa, but of the axillary portion of the capsule shortened by cicatricial contraction in its relaxed condition.

This bursa is circumscribed to the upper surface of the greater tuberosity of the humerus and the adjacent small portions of the rotators inserting into it. When the bursa is inflamed the diagnosis should be easily made by the acute tenderness localized to the upper surface of the humerus, directly in front of the acromion, when the arm is in the position of rest, that is, adduction and internal rotation, which it practically always occupies.

The capsule lesion is typified by that which occurs in an anterior dislocation of the shoulder, the frequency of which is nearly as great as that of all other dislocations of the shoulder combined. Those cases of stiff and painful shoulder in which there is no history of dislocation are explained, in the first place, by the spontaneous reduction of many dislocations as the arm falls from its abducted position to the side of the body, so that they are not recognized as such; and in the second place by the much greater frequency of milder but similar tears (sprains) from forced abduction, which are not sufficiently extensive to permit the occurrence of a dislocation.

Sprains are rarely recognized in this joint, because they are peculiarly obscure as to their etiology and symptomatology. At the moment of the forced abduction the patient is excited and does not appreciate the relation between this movement and the pain it produces, the capsule being poorly supplied with nerves and the pain of the moment probably slight. The arm immediately drops to the side into the position of most complete relaxation of the torn portion of capsule, and is kept there afterward because of the pain produced by abduction and external rotation which drag on the seat of injury. The lesion is deeply seated and localized with difficulty, and the disturbances which follow are misinterpreted.

The most rational method of treatment is that which aims at increasing the length of the contracted tissues to the normal, favors the absorption of inflammatory material, and increases the power of the weakened and atrophied muscles.

THE INTERRELATION OF THE ORGANS OF INTERNAL SECRETION.¹

II. THE PITUITARY

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THE PITUITARY. It has seemed best to discuss the pituitary as a single organ, since it is very generally so treated in the literature; but this is on the score of convenience merely since in its two lobes we are dealing with entities of distinct origin and different functions. This structure will be considered in relation to the thyroid, the reproductive organs, the adrenals, and the pancreas.

Pituitary-thyroid Hyperpituitism. The effect of experimental hyperpituitism upon the thyroid has been as yet but little studied—largely, probably on account of the difficulty of obtaining pituitary material. That a condition parallel to true hyperactivity of the normal gland can be secured by the injection of extracts or by feeding gland substance is by no means so sure as in the case of the thyroid. Hallion and Alquier² subjected five rabbits to prolonged ingestion of extracts of the pituitaries of cattle, using the whole gland. At autopsy the thyroids were found to contain less than the usual amount of colloid, and the cells were somewhat more nearly columnar than normal. Rénon and Delille³ obtained the same results, using intraperitoneal injections of extracts of the gland. They found that the use of the posterior lobe alone had effects similar to the use of the whole gland. This result is incidentally in harmony with the usual results reported by other investigators, who have uniformly found extracts of the anterior lobe without physiological effect. Both sets of experiments indicate that the active substance of the pituitary has a slightly stimulating effect on the thyroid. Lucien and Parisot,⁴ however, have repeated the experiments of Rénon and Delille and obtained somewhat different results. They noted a hypertrophy in the thyroids of from 10 to 40 per cent., with an increased amount of colloid—an appearance “hardly indicating increased activity, but rather resembling a simple goitre.” Sandri⁵ found in guinea-pigs that feeding or injecting pituitary extracts caused in other organs no demonstrable effect whatever. Similar results have been obtained by the writer in case of nineteen young guinea-pigs. The evidence, therefore, on the whole, is inconclusive.

¹ Concluded from page 385.² Comp. rend. Soc. de biol., 1908, lxxv, 5.³ Ibid., lxxv, 499.⁴ Ibid., 1909, lxxvi, 675.⁵ Arch. ital. de biol., 1909, li, 337.

Hypopituitarism. The little existing evidence as to the effects of deficiency of pituitary secretion upon the thyroid, is positive and clear cut. Cushing,⁶ after an extensive study of the results of hypophysectomy in young dogs, states explicitly that the operation causes acute hypertrophy of the thyroid. An instructive study has been made by Exner,⁷ of two of Hochnegg's surgical cases, that were essentially experiments bearing directly upon this point. In both instances the pituitary had been extirpated for the relief of akromegaly, and later there was found, among other results, an undoubted hypertrophy of the thyroids.

These results bear a suggestive similarity to the effect of thyroidectomy upon the pituitary and justify an extension of the theory of vicarious activity to include both glands. The theory implies that the glands are more or less synergic. The hypothesis is further supported by the observations of Soli⁸ that after castration in all but 5 of 25 cases, hypertrophy of the pituitary occurred; in these 5, the *thyroids* were enlarged. Taken altogether, the evidence supports a theory that the two glands are synergic and either can to some extent, in case of need, function vicariously for the other.

Pituitary; Gonads. Clinical observers have noted that disturbances of pituitary function—either by tumors in the gland itself, or by pressure of brain tumors near it—are frequently associated with sexual anomalies.^{9 10} Cessation of menstruation in the female and impotence in the male are recognized initial symptoms of akromegaly,^{11 12} and the same effects are noted when neoplasms exert pressure upon the hypophysis.¹³ The two previously mentioned cases of akromegaly described by Exner are especially significant in this connection. The onset of the disease in each instance was marked by the development of amenorrhœa. The restoration of menstruation after the removal of the tumors indicates a specific causal relationship of the pituitary conditions. Thumin¹⁴ has reported the case of a young woman whose sexual functions became erratic with the development of a pituitary tumor, and whose ovaries atrophied as the disease progressed. Other cases of adults of both sexes, in whom atrophy or aplasia of the gonads (infantilism) has been associated with pituitary tumors, have been described by Cushing,¹⁵ Schuller,¹⁶ Kon, v. Eiselsberg, and

⁶ Jour. Amer. Med. Assn., 1909, liii, 249.

⁷ Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1909, xx, 620.

⁸ Arch. ital. de biol., 1910, lii, 353.

⁹ Kon. Beitr. z. path. Anat., 1908, xlv, 233.

¹⁰ Church. Jour. Amer. Med. Assn., 1909, liii, 97.

¹¹ Cagnetto. Virch. Arch., 1908, clxxxvii, 197.

¹² Kon. Beitr. z. path. Anat., 1908, xlv, 266.

¹³ Axenfeld. Neurol. Centralbl., 1908, xxvii, 608.

¹⁴ Berl. klin. Wochensh., 1909, xli, 631.

¹⁵ Amer. Jour. Nerv. and Ment. Dis., 1906, xxxiii, 704.

¹⁶ Neurol. Centralbl., 1907, xxvi, 965.

v. Frankl-Hochwart,¹⁷ Rénon, Delille, and Monier-Vinard,¹⁸ and by Schloffer.¹⁹ A particularly instructive case has been reported by v. Eisel berg;²⁰ a young man, aged twenty years, developed a typical case of *degeneratio adiposogenitalis*, with a tumor of the pituitary, and infantile sex organs. The tumor was successfully removed, and a year later, marked genital development had occurred.

Clinical evidence of this nature supports rather convincingly a conclusion that there is some sort of coördination between the activities of the hypophysis and of the gonads. The actual significance of the data, however, is obscured by the uncertainty that prevails as to the etiology of akromegaly. The disease is usually ascribed to hyperplasia of the pituitary, that is, to *hyperpituitism*, but the effect upon the gonads is often the same as that of obliterative tumors, that is, of *hypopituitism*.

Hyperpituitism. As mentioned before, few experimental observations upon the effects of hyperpituitism have been reported. None in which the gonads were considered are known to the writer, except those previously discussed by Hallion and Alquier, Rénon and Delille, and Sandri. As regards the sex glands, negative results were reported in each case.

Hypopituitism. The evidence as to hypopituitism is likewise meagre. Although many partial and complete hypophysectomies have been made, but little attention apparently has been paid to the effects upon other organs of internal secretion. Cushing, however, has noted that after extirpation of a part of the anterior lobe, the gonads often atrophy. It is interesting to note that a tendency to obesity, such as is observed after castration, also occurs. This evidence, together with the observed effect of obliterative tumors in the hypophysis region, indicates that the pituitary normally supplies a secretion that stimulates the sex glands to activity. More definite experimental evidence is needed, however, before a final conclusion can be reached.

Pituitary; Adrenals. The observations regarding a relationship between the pituitary and the adrenals are few. Hallion and Alquier have noted hyperplasia of the adrenal cortex after prolonged feeding of pituitary extract. After intraperitoneal injection of a similar extract, Rénon and Delille have obtained the same result. In both cases the posterior lobe alone was effective. No other data upon this relationship have been found in the literature. Any valid conclusion, therefore, in regard to the matter is obviously impossible.

Pituitary; Pancreas. Whether there is any direct relationship between the pituitary and the pancreas is doubtful. Glycosuria

¹⁷ Wien. klin. Wochens., 1908, xxi, 1115.

¹⁸ Bull. et Mem. Soc. Med. de hóp. de Par., 1909, xxvi, 204.

¹⁹ Wien. klin. Wochens., 1907, xx, 621.

²⁰ Neurol. Centralbl., 1907, xxvi, 994.

frequently occurs in akromegaly. Sternberg²¹ regards this as due to changes in the pancreas. Benda,²² however, thinks that there is no constant change in the pancreas in akromegaly, even in diabetic cases.

The evidence as a whole, indicates a mutual relation between the thyroid and the pituitary such that deficiency of the one leads to increased activity of the other. This is due to the vicarious assumption by the one, of the depressed function of the other. A tentative conclusion that the pituitary exercises a normal stimulating effect upon the sex glands is justified. The meagre data available indicate that the adrenals are stimulated by pituitary secretion, but give little weight to the conclusion. Whether the pituitary has any direct relation with the pancreas is questionable.

THE ADRENALS. The so-called "adrenal gland" consists of two parts, the cortex and the medulla, which are very probably physiologically independent structures. The only known active substance that has been demonstrated in the adrenals is produced entirely by the medulla. The two parts are of different embryonic origin, and in some of the lower fishes, they remain distinct throughout life. A separate consideration of the two parts would be desirable, therefore, in this work, but this would not be feasible because in the literature a distinction has not been consistently observed.

Adrenals; Gonads. A theory that the adrenals are related to the sex function was proposed by Meckel,²³ as early as 1806. It was based upon the following grounds: (1) In certain aborted fetuses he had noted that both the adrenals and the gonads were lacking; (2) in animals in which sexuality is marked, such as the guinea-pig, the adrenals are notably large; (3) in birds and amphibia the gonads and adrenals are closely associated in position, and (4) he had noted adrenal degeneration in several cases of diseases of the genitalia. Meckel's evidence has been controverted by various writers, notably by Nagle,²⁴ but the idea has persisted and at the present time there exists considerable evidence in its favor. This is partly clinical and partly experimental.

In cases of hermaphroditism, marked hypertrophy of the adrenals is sometimes observed. Instances of this association of conditions have been reported in detail by Creech²⁵ and by Marehand.²⁶ v. Nengebauer²⁷ in an extensive review of the literature of hermaphroditism published in 1908, was able to find record of 13 cases in which this association was mentioned. As evidence these few instances have no great weight, but they are suggestive.

²¹ "Akromegaly," Nothnagel's Handbuch d. spec. Path. u. Ther., vol. vii, Band 2.

²² Cited by Dock; Osler's Modern Medicine, 1909, vi, 468.

²³ Cited by Nagle.

²⁴ Wien. med. Presse, 1866, p. 763. Cited by Bullock and Sequiera.

²⁵ Festschrift f. R. Virchow, i, 574.

²⁶ Hermaphroditismus beim Menschen, Leipzig, 1906, p. 685.

²⁷ Müller's Arch., 1836, p. 365.

Bullock and Sequiera²⁸ have been able to find in the clinical literature 12 cases of children showing sexual precocity, who at autopsy, were found to have enlarged adrenals; 10 of these were females, from two to eleven years of age, and 2 were males, aged five and fifteen years respectively. In view of the fact that comparatively a small proportion of such cases come to autopsy at a time when the condition is recognizable, these findings are of some weight as indicating adrenal activity as a condition of sexual development.

Various other instances of associated sex and adrenal anomalies have been recorded. Otto²⁹ noted in a patient a simultaneous hypertrophy of the gonads and the adrenals. Wiesel³⁰ and Karakascheff³¹ have each reported an instance of adrenal atrophy accompanied by sex depression, and Bullock and Sequiera mention 3 others. Borz³² and Thumin³³ have recently described 2 cases of young women who had been sexually normal up to the age of sixteen years and in each of whom then, menstruation ceased; the voice became coarse, and an extensive growth of hair upon the body occurred. At autopsy both were found to have markedly enlarged adrenals. In Thumin's case, the ovaries were somewhat atrophic.

The clinical literature taken altogether indicates that there is a correlation between the adrenals and the gonads. It further suggests, too, a theory that the adrenals furnish a stimulus to the gonads. Such a theory, however, is susceptible to the general objection that associated conditions in the two organs may be effects of some common influence, and neither the cause of the other.

The truth of the theory has been tested but little by experimentation. It has been noted by Bossi³⁴ that goats can go through pregnancy and give birth to normal young after the removal of one adrenal. Hultgren and Anderson³⁵ have found the same to be true of the guinea-pig. The writer has noted, however, that from a given number of guinea-pigs so treated, even though they appear perfectly healthy, the number of offspring secured in the course of a year is notably below normal. Landau³⁶ states that adrenal extirpation is without demonstrable effect upon the ovaries of adult rabbits. Since bilateral adrenal extirpation is rapidly fatal, however, and unilateral extirpation is notably ineffective

²⁸ Trans. Path. Soc., London, 1905, iv, 189.

²⁹ Pathol. Anat. Beobachtungen, p. 139. Cited by Bullock and Sequiera.

³⁰ Virch. Arch., 1904, clxxvi, 103.

³¹ Beitr. z. path. Anat., 1904, xxxvi, 401.

³² Arch. f. Gyn., 1909, lxxxviii, 445.

³³ Berl. klin. Wochensh., 1909, xlv (1), 103.

³⁴ Arch. f. Gyn., 1907, lxxxii, 505.

³⁵ Skand. Arch. f. Physiol., 1899, ix, 73.

³⁶ Experimentelle Nebennieren-studien, Dorpat, 1908.

negative results are of slight significance, and scarcely modify the conclusion reached from a study of the clinical literature.

Adrenals; Thymus. The relation of the adrenals to the thymus has apparently received little attention, and there is some likelihood that the clinical evidence is defective simply for this reason. In 1902, Pansini and Bonenati described a case of Addison's disease in which in addition to the characteristic adrenal degeneration there was a marked hypertrophy of the thymus. In 1904, Wiese described a second case. In his report he discussed at some length the association of adrenal hypoplasia and thymus hypertrophy, and claimed priority for the discovery that such an association is common in cases of *status lymphaticus*. In view of this asserted relationship, Hedinger,³⁷ in 1907, made a study of all the material from cases of Addison's disease available in the pathological institutes of Berne and Basel, and found in a majority of the cases a recognizable condition of *status lymphaticus*. Other cases of this association have since been reported by Hart,³⁸ Pappenheimer and Kahn.³⁹ The clinical data are consistent so far as they go, but further observations are needed.

Very little experimental work upon the subject has been done. Boinet⁴⁰ at the autopsies of rats that had survived for a considerable length of time the extirpation of both adrenals found that 11 of 50 individuals showed thymus hypertrophy. Auld,⁴¹ in 1899, in an investigation of "compensatory hypertrophy" found in each of four cats upon which he had performed unilateral adrenal extirpation a "very great hypertrophy" of the thymus. Other investigators who have performed epinephrectomies seem not to have paid attention to the condition of the thymus. The possible results in the thymus after this operation may have been overlooked because the animals either die within a short time, or if they survive long, become more or less cachectic. In the first condition, time would not have been allowed for hypertrophy to occur, and in the second, any tendency to hyperplasia would be masked by the marked tendency of the thymus to atrophy in case of deficient nutrition.⁴²

On the whole, it appears that adrenal deficiency is frequently associated with hypertrophy of the thymus, and so far as the evidence bears upon the point, that is, in Addison's disease, and in experimental adrenal deficiency, that the condition in the adrenals is primary to that in the thymus. More evidence is needed, however, before any final conclusion can be reached.

³⁷ Verhandl. d. deutsch. path. Gesellsch., 1907, xi, 29.

³⁸ Wien. klin. Wochensh., 1908, xxi, 1110.

³⁹ Virch. Arch., 1910 (June).

⁴⁰ Comp. rend. soc. de biol., 1895, xlvii, 163.

⁴¹ Brit. Med. Jour., 1899, p. 1327.

⁴² Jonseri, Arch. f. mikr. Anat., 1909, lxxiii, 390.

Adrenals; Pituitary. The observations as to a relationship between the pituitary and the adrenals have been few. Boinet, in experiments previously mentioned, found pituitary hypertrophy following epinephrectomy in 4 only of 50 cases. Alquier observed also, in a dog, slight evidence of hypertrophy after the same operation. A similar effect in the guinea-pig, dog, and cat, has been noted by Marenghi.⁴³ Landau has found that in the adult rabbit adrenal extirpation is entirely without effect upon the hypophysis. At present, therefore, there is little evidence of any relationship of the adrenals to the pituitary.

Adrenals; Thyroid. Whether a demonstrable result in the thyroid follows adrenal extirpation is questionable. Boinet found hypertrophy of the thyroids in 12 of 50 cases. Landau, however, who has investigated the matter at some length, states that in his experience, adrenal extirpation has upon the thyroids no effect whatever. Parhon and Goldstein⁴⁴ noted in three dogs an augmentation of colloid in the thyroids after a short course of treatment with adrenalin. No definite conclusion in regard to this relationship is yet possible.

Adrenals; Pancreas. Previous mention has been made of Eppinger, Falta, and Rudinger's hypothesis that the chromaffin system and the pancreas are mutually antagonistic. An adequate discussion of the theory would necessitate a review of a long series of researches such as the scope of the present work scarcely permits. Their conclusions as regards the pancreas are based upon the fact noted by Blum, Zülzer and others that the injection of adrenalin causes glycosuria. The theory has the weakness inherent in our ignorance of many of the details of carbohydrate metabolism. It is supported by the observations of Rudinger, Falta, Eppinger, Pollak, and Porges⁴⁵ that in Addison's disease the dextrose limit is high. A final evaluation of the theory, however, must await the accumulation of more evidence.

In summary it appears that the theory of an association between the activities of the adrenals and the gonads is well supported, and there is some reason to believe that the former glands may stimulate the latter. Adrenal hypoplasia and thymus hyperplasia are frequently associated; probably the former condition stands in causal relationship to the latter. There is little evidence of a relationship of the adrenals to the pituitary. The theory that the adrenals stimulate the thyroids has some evidence in its favor but more data are needed; the same is true of the hypothesis that the adrenals inhibit the pancreas.

THE GONADS. While it is probable that the testes and ovaries, considered as organs of internal secretion, have little in common, it will be more convenient to consider them together.

⁴³ Lo Sperim., 1903, lvii. Cited by Alquier, p. 494.

⁴⁴ Rev. neurol., 1909, xvii, 1143.

⁴⁵ Zeit. f. klin. Med., 1910, lxx, 243.

*Gonads; Pituitary; Hypergonadism.*⁴⁶ No evidence has been found of any effect of activity of the male sex organs upon the pituitary. In the female, pregnancy has been observed to cause an increased activity of this gland. Launois and Mulon,⁴⁷ Morand, and Guerrini,⁴⁸ and Laignel-Lavastine have reached that conclusion from cytological studies. The matter has recently been determined conclusively by Erdheim and Stumme,⁴⁹ who have found from a careful comparison of the weights and cytological condition of the pituitaries from 85 pregnant women with 13 from nulliparæ that both pituitary hypertrophy and increased cellular activity accompany pregnancy. Whether this effect, however, is due to sexual activity *per se* is open to question. The increased activity may be simply a reaction to the changed metabolic conditions that undoubtedly occur during pregnancy. Laignel-Lavastine states that hyperemia and hypertrophy of the pituitary can be demonstrated during menstruation, but the assertion lacks corroborative evidence. Rénon and Delille⁵⁰ have reported that ovarian extract "moderates the pituitary" but their evidence is not convincing. No definite conclusion, therefore, can as yet be reached as to whether or not hyperactivity of the sex glands has any effect upon the pituitary.

Hypogonadism. The effects of castration upon the pituitary have been studied by several investigators. Ceece⁵¹ has reported entirely negative results in both sexes; since, however, the details of his research are not given, a critical consideration of his work is not possible. Fischera⁵² has studied the matter in 65 animals—cocks, 50; buffalo, 5; cattle, 5; guinea-pigs, 2; and rabbits 3 cases—and has found that castration in both sexes is followed by an undoubted hypertrophy of the anterior lobe of the pituitary, with a hyperplasia of the eosinophile cells. In three capons he found that injections of testicular extracts caused a rapid disappearance of the eosinophilic substance. Fischera's results seem well established and have been generally accepted as valid. His findings have been confirmed by Tandler and Gross,⁵³ by Soli, and by Schutz,⁵⁴ on animals and somewhat doubtfully by Kon in a study of the pituitaries of 7 women, and of 1 man, after surgical castration. The effects of this operation seem to be confined to the anterior lobe. These observations suggest that the pituitary may normally be held in check by secretions of the gonads, and

⁴⁶ "Hyper-" and "hypogonadism" are proposed as terms to indicate conditions due to excessive and depressed secretory activity, respectively, of the gonads considered as organs of internal secretion.

⁴⁷ Arch. de gyn. et Obst., 1904, p. 1.

⁴⁸ Zeit. f. allg. Path. u. path. Anat., 1905, xvi, 177.

⁴⁹ Beitr. z. path. Anat., 1909, xlv, 1.

⁵⁰ Comp. rend. soc. de biol., 1909, lxxvi, 89.

⁵¹ Arch. ital. de biol., 1905, xliii, 403.

⁵² Cited by Cushing; Amer. Jour. Med. Sci., 1910, cxxxix, 478.

⁵³ Presse Méd., 1904, xii, 341.

⁵⁴ Wien. klin. Woch., 1908, xxi, 289.

that when this inhibition is removed, the pituitary manifests increased activity, leading to altered metabolisms and thus to an overgrowth of different parts of the body, such as occurs both in akromegaly, and after castration.

Gonads; Thymus. The evidence of a relation between the gonads and the thymus is not extensive, but is entirely concordant. That the thymus persists until puberty, when the sex glands undergo a physiological hypertrophy, has long been known. It would be *a priori* likely, therefore, that castration, would tend to prolong the persistence of the thymus. The facts bear out the supposition. Calzolari⁵⁵ apparently was the first to investigate the matter experimentally. In six castrated rabbits he found that the thymus invariably attained greater weight and persisted longer than in normal animals. Henderson⁵⁶ investigated the matter in 114 cattle that were being slaughtered for beef. They had, of course, been castrated while young. They were found generally to have persistent thymuses. The same fact was noted by Henderson in guinea-pigs and rabbits. It was noted, also, that in cattle of both sexes, that had exercised the reproductive function, the normal thymus atrophy was accelerated. Godall,⁵⁷ in a histological study of the effects of castration in the thymus of the guinea-pig, noted that both the lymphoid tissue and the corpuscles of Hassal share in the delayed atrophy. Soli in 10 rabbits and 15 capons has noted a similar thymus persistence after castration, and Tandler and Gross have found the same effect in roebucks, dogs, and goats. These writers state also, that persons with hypoplastic gonads retain their thymuses longer than normal. It can, therefore, be definitely asserted that the gonads exert a depressing effect upon the thymus.

Gonads; Adrenals. The effect of conditions in the gonads upon the adrenals has not been studied to any great extent. Guieysse⁵⁸ and Marrassini⁵⁹ have noted that in guinea-pigs the adrenals enlarge during pregnancy, but as pointed out previously, the interpretation of this condition as primarily a sex phenomenon is questionable. Cecca, Marrassini, and Tehodossier⁶⁰ have reported that hypertrophy occurs in the adrenal cortex after castration just as it occurs in the pituitary after the same operation. These observations have been confirmed by Soli. He has noted further that the hypertrophy is succeeded by an atrophy. This paucity of data, however, permits no final deduction as to the effects of conditions in the gonads upon the adrenals.

Gonads; Thyroid. But little is known of the effects of the gonads upon the thyroid. So far as has been discovered in the present

⁵⁵ Arch. ital. de biol., 1898, xxx, 71.

⁵⁶ Jour. Physiol., 1904, xxxi, 222.

⁵⁸ Comp. rend. soc. de biol., 1899, xlix, 89S.

⁵⁹ Arch. ital. de biol., 1906, xlvi, 73.

⁶⁰ Russky Vratsch., 1906, No. 5. Cited by Borz.

⁵⁷ Jour. Physiol., 1905, xxxii, 191.

investigation the effects of testicular extracts upon this gland have never been studied. Ovarian extract injected intraperitoneally has been observed by Rénon and Delille to cause congestion or even hemorrhage in the thyroid; such an observation, however, is probably of slight significance as indicating any definite relation between the two glands. The thyroid often hypertrophies during menstruation and pregnancy, and this is sometimes interpreted as indicating a relation between the ovaries and the thyroid. Most observers have failed to note any effect of castration upon the thyroid, but Cecca and Delille, have noted in both sexes a hypertrophy. Soli observed no effect upon the thyroid of this operation in cocks, but in rabbits for the first three months there was a slight augmentation, followed later by a depression of the thyroid weights. The evidence altogether is too meagre in quantity, and conflicting in tenor to permit any conclusion as to a possible effect of the gonads upon the thyroid.

It appears that hypogonadism leads to hypertrophy of the pituitary possibly by removing a normal check upon it; activity of the sex glands seems to lead to depression of the thymus. A few observations indicate that the adrenal cortex hypertrophies after castration. The evidence as to the effects of activities of the sex glands upon the thyroid is meagre and not concordant.

THE THYMUS. Despite a great deal of work upon the subject, little is known of the function of the thymus, and of the data available few observations bear upon the relation of the organ to other glands. Previous mention has been made of the hypertrophy of the thymus that occurs in cases of Addison's and of Graves' diseases but the significance of the condition is unknown.

Thymus; Gonads. Paton⁶¹ has reported that removal of the thymus in young guinea-pigs causes a more rapid growth of the testes than normal. Soli, however, has obtained in cocks and rabbits exactly the opposite effect. Whether the thymus, therefore, has any influence upon the sex glands remains an open question.

Thymus; Thyroids. Aside from a report by Lucien and Parisot⁶² that a series of rabbits killed at varying periods after thymectomy had in every case smaller thyroids than the controls, there is no evidence known to the writer of a relation of the thymus to the thyroid. Soli after a series of 34 thymectomies found no demonstrable effect in the thyroids. In some cases he observed a slight but probably negligible augmentation of the weights of the pituitaries, and of the adrenals.

THE PANCREAS. Previous mention has been made of Falta's theory of the antagonism between the pancreas and the thyroids. There is little direct evidence that the pancreas does depress thyroid activity. Licini⁶³ has noted in dogs, however, a pro-

⁶¹ Jour. Phys., 1904, xxxii, 28.

⁶² Deutsch. Zeit. f. Chir., 1909, ci., 522.

⁶³ Comp. rend. soc. de biol., 1909, lxvi, 406.

gressive hypertrophy of the thyroids with an increase in the colloid content after pancreas extirpation. The histological appearance of the thyroids in his opinion indicated an increased functional activity.

THE PARATHYROIDS. There is but little known of the relationships between the parathyroids and other endosecretory organs. Marinesco and Parhon⁶⁴ have noted after thyreoparathyroidectomy a marked increase in the fat-like material in the cells of the adrenal cortex. This change they at first ascribed to the removal of the thyroid, but after a repetition of their experiments, concluded that it was caused mostly or wholly, by the loss of parathyroid tissue. Caro and others have postulated an antagonism between the parathyroids and the thyroids, adrenals, and pituitary, on the grounds that the parathyroids depress the irritability of the nervous system, carbohydrate metabolism, calcium, and magnesium metabolism, and blood pressure. There is, however, little or no direct evidence on the point.

THE PINEAL BODY. There is some slight evidence that the pineal body may have an influence on the development of the gonads. Raymond and Claude⁶⁵ have recently reported in detail one instance and cited a few others of pineal tumors associated with sexual precocity. Such instances are too rare, however, to have any great significance.

In this work little mention has been made of the possible mechanisms by which the various effects described have been produced. Very suggestive is the work of Falta, Kostlivy, Caro, and others, which indicates that many of the symptoms of endosecretory disturbances are due to stimulation of the sympathetic and general autonomic nervous systems—sometimes acting concordantly, sometimes antagonistically. Other effects may be reactions to endotoxins due to perverted metabolisms. Others are probably due to direct hormone stimulation of various organs. Before the mechanisms of the various interactions can be fully understood, a much greater number of definite data must be secured.

The writer is aware that in the attempt to collect the evidence from such widely scattered sources, some significant observations may have been overlooked. He ventures to hope, however, that not enough has been missed to alter substantially the conclusions reached.

It is a sincere pleasure to acknowledge many obligations to Professor Walter B. Cannon for his helpful criticisms of this work.

⁶⁴ Roumanie Med., 1908, Nos. 10 and 11, 19 and 20.

⁶⁵ Bull. acad. med., 1910, lxxiv, 261.

THE SUDDEN ONSET OF PARALYSIS IN POTT'S DISEASE WITHOUT DEFORMITY OF THE VERTEBRÆ.

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COMPRESSION of the spinal cord causing paralysis may be due to various morbid processes, but here I shall refer only to compression following tuberculous caries of the vertebræ or Pott's disease. Although both the clinical and pathological manifestations of this disease have been carefully studied, there are still many disputed points in regard to the exact means by which interruption of the functions of the spinal cord are brought about, so for this reason, and on account of some very unusual features the following cases seemed worthy of careful study. I wish particularly to express my thanks to Dr. Spiller, Dr. Mills, and Dr. Frazier who have kindly furnished me with the material upon which this investigation is based.

CASE I.—A colored male, aged thirty-eight years, was admitted to the Philadelphia Hospital in the service of Dr. C. K. Mills, November 7, 1904, complaining of paraplegia. His family history revealed nothing of importance. He denied syphilis. On August 7, 1904, he became very constipated, not having had a bowel movement for fourteen days; at the same time he had considerable abdominal pain. After evacuation of the bowels by means of purgatives, the pain subsided but still lingered. About one month later his right leg suddenly gave way while walking, associated with cramp-like pain. The pain persisted two days, and then the right leg became totally paralyzed. One week later the left leg was similarly affected but without pain. Again he became very constipated and had some difficulty in urinating. Since that time the patient has been confined to bed, and he says that he has not been able to feel anything in either lower extremity. Occasionally he had girdle sensation.

The following notes were made on the day of admission: The patient is fairly well developed. He can wrinkle his forehead evenly on both sides. The nasolabial folds are of equal prominence, he can show teeth, whistle, and draw mouth back on either side. The masseter and temporal muscles contract promptly. There seems to be some wasting of the face but it is symmetrical. Both pupils are round and equal and react promptly to light and accommodation. Sensation for touch and pain is normal over the face and neck. The extra-ocular muscles are normal. Motion

and resistance to passive movements and grasp of hands is good on both sides. There is very slight ataxia of both upper limbs as shown by the finger to nose test. Sense of position is normal on both sides and sensation for touch, pain, heat, and cold is normal in the upper limbs. The lungs are hyper-resonant anteriorly and harsh breath sounds are heard over the upper portions. No rales can be elicited. The heart is normal. The abdomen is somewhat distended but not tympanitic. Palpation elicits no pain or tenderness. The abdominal organs seem normal. Sensation for touch and pain is normal over chest and abdomen; sensation for heat and cold is normal down to a point two inches below the umbilicus but below this level thermal sense is lost. There is marked atrophy of both lower limbs. Motion and resistance to passive movements is nil in both limbs. Patient is unable to move even toes. There is double foot drop. Impossible to test for ataxia on account of paralysis. Both limbs are slightly spastic, the left more so. At intervals there are involuntary contractions of the flexor and adductor muscles of each thigh. The right knee jerk is exaggerated, the left seems normal or slightly decreased. Ankle clonus is present on both sides, but it is much more persistent on the right. Babinski reflex is distinct on both sides. Sensation to touch is normal, on the left limb except for space extending downward six inches from the middle of the leg from that point downward it seems to be diminished, on the right side it is present, but the man is unable to locate touch on leg. Sensation to pain is present on the right limb but is diminished and he is unable to locate pin pricks. Sensation to pain on the left side is about the same as on the right. Sensation to heat and cold is absolutely lost over the whole of both lower extremities. Achilles jerk is absent on the right, but present on the left.

Two days later a slight angular deformity was discovered corresponding to the ninth thoracic vertebra. On November 22, all forms of sensation including touch, pain, and temperature were lost over both lower extremities and extended upward as far as the level of the umbilicus. A large bed sore had developed over the sacral region. The patient died November 30. The autopsy was performed the next morning.

Anatomical Diagnosis. Bilateral pleural adhesions, obliterative pericarditis, chronic fibrous tuberculosis of the lungs, malposition of the left kidney, gastrectasis, and enteroptosis, miliary tuberculosis of liver, dilatation and ulceration of œsophagus, subphrenic abscess, caries of lower thoracic vertebræ, tuberculous external pachymeningitis, internal hydrocephalus.

Microscopic examination of the lower thoracic segments where the pressure was greatest showed that the outline of the cord was not altered. The pia was slightly thickened on the anterior aspect, the adventitia of the pial vessels was less compact than normal

and was infiltrated with small round cells. Here and there the pia was separated from the cord, the spaces between containing a few round cells and red blood corpuscles. In the white matter the neuroglia cells were swollen and increased in number; and the glia septa were thickened, standing out prominently. Many granular cells and a few round cells were seen diffusely scattered. The white matter presented the characteristic vesicular appearance. The medullary sheaths were distended, many axis cylinders had entirely disappeared and others were swollen or atrophied. The bloodvessels were thickened and there was moderate perivascular round-cell infiltration. Although the white substance was severely diseased the area of the lateral pyramidal tracts was perhaps more affected than the other parts. The central portions of the gray matter were entirely destroyed, including all of the gray commissures and part of the anterior horns, leaving a large irregular cavity with ragged edges containing debris, few small round cells, red blood corpuscles and compound granular cells. In the remaining portions of the gray matter there were scattered round cells and an occasional granular cell. Here the bloodvessels were also thickened, and there was moderate perivascular infiltration. The necrotic cavity did not extend beyond the limits of the eighth dorsal segment but the central canal in the adjoining sections above and below was distended and the ependyma cells were partially destroyed.

In the upper dorsal, cervical, and lower lumbar segments there was some thickening of the bloodvessels within the gray matter and slight perivascular infiltration. This was more marked in the branches of the anterior spinal artery near the base of the anterior horns. With the Weigert method there was degeneration of Goll's column extending upward into the cervical region. In the lower lumbar segments no distinct degenerations were found. At the level of compression many ganglion cells within the gray matter had been destroyed but a few remained which appear swollen, and with the Weigert stain the nuclei were indistinct. The Nissl stain could not be used. The bloodvessels of the pia about the pons and medulla seemed somewhat thicker than normal and some showed slight perivascular infiltration. The cells of the choroid plexus about the fourth ventricle were very much swollen and the bloodvessels were thickened. Sections of the cerebral cortex presented some rather doubtful round cell infiltration of the pia.

CASE II.—J. D., was admitted July 16, 1904, to the service of Dr. Spiller, complaining of paralysis of both lower extremities. Three years previously his left leg had been amputated six inches below the knee as a result of injury. He denied syphilis. His family history was negative. July 2, 1904, he was compelled to go to bed on account of severe dull aching pain just below the

angle of the scapula. Two days later there was much numbness and tingling just below the painful areas and on that day he suddenly lost power in both lower extremities. During this time he had had retention of urine and was constipated.

The following notes were dictated two days after his admission: The patient is fairly well nourished. Pupils are round and equal and react promptly to light and accommodation. The extra-ocular muscles are normal. Facial muscles contract equally and promptly; movements of upper extremities are equal and normal. The epigastric and abdominal reflexes are absent on both sides. Cremasteric reflex is absent on the left and diminished on the right. The knee jerks and Achilles jerks are absent on both sides. There is no ankle clonus on either side. Sensation for pain and touch is lost over both legs and abdomen up to a point two and one-half inches below the right nipple, and about one inch lower down on the left side. Adjoining this line above is a zone of hyperesthesia about two inches wide, which narrows to about one inch in width near the axilla of either side. Testicular pain is absent.

The following additional notes were dictated by Dr. Spiller some days later: Sensation for touch, pain, and temperature is similar to the above. Cremasteric reflex is present on both sides but diminished. Passive movement of the stump of left leg on thigh causes involuntary jerking movement of this limb of which the patient is not conscious without seeing it, but he is conscious of a jarring sensation in his back. These involuntary movements are not distinct in the right lower limb. He has no knowledge of the sense of position of his legs. The knee jerks are both absent, the plantar reflex is present on the left side, but sluggish on the right. There is an area of tenderness of the spinous processes about the level of the spines of the scapula, but no deformity.

The patient died July 28, 1904.

Macroscopic examination of the spinal cord and its membranes showed an external pachymeningitis extending from the lower cervical region to the upper lumbar. There was a considerable amount of necrotic cheesy material which by microscopic examination revealed the characteristic picture of tuberculous disease. Microscopic examination of sections taken from the upper thoracic portion of the spinal cord showed no diminution in its volume. When stained by the hemalum and fuchsin method there was slight cellular infiltration of the pia, and the pial vessels presented slight infiltration of the adventitia. In the white substance there were numerous vacuoles, mononuclear cellular infiltration, thickening of the bloodvessels and slight perivascular infiltration. The neuroglia cells were increased and here and there were a few granular cells. The anterior portions of the posterior columns were partially destroyed. The anterior longitudinal septum was infiltrated

with round cells and appeared more prominent than normal. In the gray substance there was moderate diffuse cellular infiltration of the mononuclear type and red blood cells as well as compound granular cells were found. The blood vessels which were cut in cross section appeared thickened, and the perivascular and periganglionic spaces were enlarged. The most marked inflammatory changes were found about the gray commissures and central portions of the anterior horns. In some sections necrosis has taken place in the area supplied by the commissural branch of the anterior spinal artery. With the Weigert method the posterior and lateral columns suffered most, and the anterior columns least. Axis cylinders had disappeared and many remaining were swollen, while here and there a few normal fibers were seen. Many of the ganglion cells of the anterior horns had disappeared, others stained poorly, and their nuclei were indistinct. In the lower thoracic lumbar and cervical segments the process was similar in the gray matter, but much less marked, while the white substance was little affected. Distinct tract degeneration was absent except for a few degenerated fibers of Goll's column. Sections of the medulla in its lower part showed very minute capillary hemorrhages chiefly in the gray matter. The brain was not examined.

CASE III.—C. M., a white female, aged fifty years, was admitted to the Philadelphia Hospital in the service of Dr. Spiller complaining of weakness of the lower limbs. Syphilis was denied. Three months previous to admission patient first developed some pain about the left shoulder which resisted all treatment. About two months later both legs began to grow weak, this gradually progressed until one week before admission when she was unable to walk or stand without assistance.

Physical Examination: The patient is much emaciated. The pupils are equal and react normally to light and accommodation. Movements of muscles of the face, tongue, larynx, and pharynx are normal. The power of the upper extremities is equal and normal. Triceps and biceps jerks are equal and normal. Both lower extremities are completely paralyzed and there is extreme contracture at the knees and hips. From time to time there are violent jerking movements at the knees. Patellar tendon reflex is normal on the left, but slightly decreased on the right. Achilles reflexes are equal and normal. Clonus is absent. There is distinct Babinski signs on both sides. Sensation for pin prick and for touch is lost over both lower extremities and abdomen as far as the fifth interspace, at this point pain and tactile sensations are impaired but not lost. Sensation for heat and cold was not tested. The vertebral column although prominent on account of emaciation showed no deformity.

Macroscopic examination showed tuberculousaries of the second thoracic vertebra and an external tuberculous pachymeningitis.

gitis beginning one quarter of an inch above the exit of the second thoracic root and extending one quarter of an inch below the exit of the third thoracic root, therefore involving the whole of the intradural portion of the third thoracic root from its exit from the cord to its exit through the dura. Microscopic examination of section taken from the third thoracic segment showed no change in contour. When stained by the hemalum and fuchsin method the pia seemed normal, but there was a slight mononuclear cellular infiltration of the adventitia of some of the pial vessels. In the white matter the walls of the bloodvessels were thickened and there was a very slight perivascular infiltration of mononuclear cells and an increase of the glia cells. There were no distinct areas of softening.

In the gray matter there were many mononuclear cells diffusely scattered. By the Nissl stain the ganglion cells were few in number and those remaining were much degenerated. With the Weigert method the medullary sheaths were swollen and many axis cylinders had disappeared. By the Marchi method nearly all the fibers of the white matter were degenerated, but a few scattered normal fibers still remained on the lateral columns near the periphery. Above and below the site of compression distinct tract degeneration was absent, though a few fibers were found staining very darkly in the pyramidal tracts and in the posterior columns by the Marchi stain.

In cases of tuberculous caries infection is generally carried to one of the vertebræ from some other focus within the body such as the lung, and a chronic osteomyelitis or periostitis ensues. This may go on to necrotic softening, and then by purely mechanical means the adjacent vertebræ above and below become approximated producing the well-known deformity of Pott's disease. In some instances this deformity may be sufficient to cause direct pressure upon the cord, but as Kraske has shown, it is uncommon; he having found it in only 6 of his 58 cases. Occasionally a subperiosteal abscess may exert pressure; Oppenheim and others have even seen cases in which spicules of necrotic bone encroached upon the cord. In the great majority of cases however, infection extends to the external lateral and posterior surface of the dura setting up a chronic inflammation which produces great thickening with epidural exudates and fungoid proliferations. Fickler in 20 cases found compression caused by dislocation of a vertebra in 9 per cent.; by abscess formation, in 17 per cent.; while pachymeningitis externa was responsible for 73 per cent. Infection of the dura nearly always arises by direct extension from a focus in one of the vertebræ, yet Schlesinger, Hennenberg, and Rossi, have each reported a very uncommon condition in which there was tuberculous pachymeningitis without caries of the vertebræ.

A similar case has recently been under the care of Dr. Spiller, and Dr. Frazier, the notes of which are as follows:

CASE IV.—H. B., a male, white, was admitted to the University Hospital, April 10, 1909, in the service of Dr. Spiller.

The patient's father, grandfather, one aunt, and one sister died of tuberculosis. Six years ago the patient had scarlet fever which was followed by paralysis of all four extremities lasting two months and then he entirely recovered. Seven months previous to admission he first developed pain in the region of the sixth dorsal vertebra. Pain was present on movement and on jarring of the spinal column, and continued in spite of treatment. About five weeks ago he noticed his legs were growing weak and that he staggered when walking. Occasionally he had cramp-like pains in the calf muscles of both legs. This condition increased gradually until two weeks ago when he was not able to walk at all. Pain still continued in the lower legs. Patient cannot control bowels and can retain urine only a short time, and is troubled with distention of the abdomen. He states that for the last four weeks he could not feel distinctly below the hips.

The following notes were dictated by Dr. Spiller: Patient is completely paralyzed in both extremities, slight movement of drawing upward of the left lower leg seems to be from muscles of the trunk. Limbs are not wasted. Patella and Achilles reflexes are about normal on each side. No ankle clonus on either side. Dr. Willard, Jr., noticed bilateral ankle clonus three days ago, before patient entered hospital. Tactile sensation seems to be preserved in all parts of the body except possibly over the front and outer side of the thighs. Here he sometimes answers incorrectly. Pain, heat, and cold sensations are lost or greatly impaired over both lower limbs and trunk anteriorly and posteriorly to a line three inches below the nipple. Area of disturbed sensation shades off gradually into an area of normal sensation. Babinski sign is typical on each side. Testing him with pin prick, or heat, and cold, causes at times either lower limb to be forcibly drawn upward. The upper thoracic vertebrae are distinctly arched, but there is no sharp kyphosis, only gradual arching. Von Pirquet tuberculin test was positive, twenty-four hours. Urine was negative. Blood count was: hemoglobin, 48 per cent.; red blood corpuscles, 4,880,000; leukocytes, 11,900.

Additional notes dictated by Dr. Spiller, May 19, 1909: Both legs are completely paralyzed. There is considerable desquamation of the skin of the feet and legs below the knee. There is involuntary drawing upward of lower limbs at hips and knees. Has imperfect control over bladder, cannot hold urine; no control over rectum. Only pain he has now is at lower costal margin, and there is no atrophy of any part of the body or even of the lower limbs. Lower limbs are very spastic. Knee jerks are

exaggerated on both sides. Patellar clonus present on both sides. Achilles jerks are exaggerated on both sides but clonus is not obtained on either side on account of spasticity. Any irritation of the limbs or trunk causes limbs to be drawn forcibly upward. Touch, pain, heat, and cold sensations are lost in the lower limbs and trunk anteriorly and posteriorly to a line drawn around the body from the eleventh and twelfth thoracic vertebræ to the sixth interspace on the left side in the nipple line, and seventh interspace on the right side in the nipple line. This line is very sharp for touch but not so sharp for pain and temperature sensations. There is no involvement of the upper limbs. Prominence of vertebræ is in the midthoracic region but no actual displacement.

On June 24, Dr. Frazier removed the fourth, fifth, and sixth dorsal spinous processes. During the operation the following notes were dictated. Coming out between the transverse processes of the fifth and sixth dorsal vertebræ was found a mass of tissue about the size of a marble presenting the appearance of granulation tissue. Upon exposure of the cord it was found free from involvement, the tumor tissue seemed to come out from either right side of the body of the vertebra or from the transverse process of the fifth dorsal. All tumor tissue that could be was removed with scissors and curette. There was evidently compression of the cord at the site of injury which was relieved by removal of the laminæ. Tumor did not make pressure over the dorsal but over the lateral aspect of the cord. Recovery after operation was good.

The pathological report was as follows: The specimen consists of laminæ and small portion of spinal meninges with nerve cord about three inches long. Microscopically, soft tissue removed from laminæ shows simple areolar tissue, the fibrous elements of which are somewhat thickened and in places infiltrated with small round cells, also a few degenerated muscle fibers are seen and many typical tubercles were found with epithelioid cells and giant cells.

On October 11 examination of the patient showed there was no return of power in the lower extremities. Sensation to pain and touch is lost below the fifth interspace on the right side anteriorly and the sixth space anteriorly on the left side. Patient complains of sharp pain in the region of the right nipple on attempting to raise head from bed.

In attempting to explain the intraspinal lesions of Pott's disease it must be borne in mind that there are two cardinal factors each of which originate outside the dura, namely, pure mechanical compression and infection. Charcot and Michaud believed that degeneration of the spinal cord was caused by infection extending into the substance of the cord setting up a secondary myelitis;

on the other hand, Kahler was able to show by compressing the spinal cords of animals with non-toxic substances that lesions similar to those following caries of the vertebræ resulted. Later Leyden, recognizing the possibilities of infection, declared that compression in itself was an important factor. Strümpell strongly opposed the myelitic theory explaining the alterations in the cord as the result of œdema stoppage of the lymph stream, and anemia, secondary to pure compression; Schmaus was inclined to accept Strümpell's view but modified it somewhat by adding that there was a collateral inflammatory œdema which could be attributed to toxic influences; more recently, however, in an article upon myelitis the same author has expressed the opinion that constant prolonged pressure upon the cord may lead not to stasis œdema but to true secondary inflammation, that is, myelitis.

The first three cases which I have described presented swelling and destruction of axis cylinders, proliferation of the glia, round-cell infiltration, sclerosis of the bloodvessels, perivascular infiltration, necrotic softening of the central gray matter, and compound granular cells at the level of greatest compression of the spinal cord. In Case I there was an internal hydrocephalus affecting only the lateral ventricles; the foramina, however, were not occluded, but the cells of the choroid plexus were decidedly diseased; it is conceivable, therefore, that as a result of perverted function of diseased cells there may have been an increase of secretion sufficient to cause this distention. But it is also possible that hydrocephalus may have been the result of compression of the cord, and that if an ophthalmological examination had been made choked disk would have been found. Choked disk has not been seen frequently in Pott's disease, yet it has been observed in spinal tumor by Bailey. At other levels of the spinal cord where compression seemed to play no part there were definite though very moderate signs of vascular disease, consequently it might seem as if there was some other element responsible as well as compression.

Spiller in an article on Pott's disease refers to a form of simple meningomyelitis without giant cells or miliary tubercles, occurring particularly when Muller's fluid had been used for preservation, he also quotes Oppenheim who had called attention to a similar type of myelitis in persons dying of generalized tuberculosis. In my cases there were no specific signs of tuberculosis found within the dura, yet the diagnosis of Pott's disease is evident, and it does not seem probable that the existence of myelitis would be disputed.

The symptoms of cord involvement in Pott's disease vary considerably in their mode of onset, but after having once begun they frequently progress rapidly. Usually the onset is chronic, the signs of paralysis requiring some months to reach their height. Occasionally paraplegia develops in the course of two or three weeks. Very rarely, however, there is an instantaneous onset,

and, moreover, in such cases there is usually a history of trauma, or some undue strain upon the diseased vertebral column immediately preceding the initial paresis or paralysis, which causes sudden displacement of one of the vertebræ and thus brings about rapid compression of the spinal cord. Gowers describes a child with angular deformity of the spine, who, while walking across the room, suddenly fell to the floor and after being lifted up was paralyzed in both legs. In Case IV not only was deformity absent, but, as far as could be determined at operation, the vertebræ were entirely normal. Deformity was entirely lacking in the other three cases at the time of the onset of paraplegia, yet in Case I and Case II the development of paralysis could not have been more rapid. In the first case, motor and sensory paralysis of one lower extremity was said to have begun instantaneously, the patient's right leg suddenly giving way under him while walking, and one week later the left leg was similarly affected. The second patient developed paralysis of both lower extremities in an equally rapid manner. Truly an apoplectiform onset in the strictest sense of the term.

After searching the literature upon this subject I have been able to find only two cases described in which paralysis developed instantaneously without deformity of the vertebræ. One case with necropsy reported by Raymond seventeen years ago seems to have been entirely overlooked, another without necropsy was described by Martineck during the past year. Raymond's case is as follows: A young girl developed complete motor paralysis of both upper extremities and incomplete motor paralysis of the lower limbs within a few hours. Laminectomy was performed and the pia was found to be thickened and the cord much congested, but without evidence of compression. The patient died on the same day and at the autopsy tuberculous caries of the third cervical vertebra and abscess formation was found. Microscopic examination showed inflammation and hemorrhage in the gray matter, sclerosis of the bloodvessels and cellular infiltration of the pia, while the white matter was much less involved, yet there were no specific lesions of tuberculosis within the dura.

Martineck's case was that of an adult male, who had been complaining for some months of severe pain. The patient went to bed feeling generally weak, the next morning there was paresis of both legs, by the afternoon there was paralysis of both lower extremities. When the patient was seen at the hospital the following day there was almost complete motor paralysis and involvement of the bladder, still the vertebral column showed no abnormality. There was neither tenderness nor pain on movement. It was not until eight days after paralysis had developed that an angular deformity was discovered extending from the eighth to the eleventh dorsal vertebræ. X-ray examination showed abnormality in the position of the ninth dorsal vertebra.

When the term myelitis is used in its strictest sense to mean inflammation of the spinal cord, Russel believes that it is a rare disease, and attributes much of which we speak of as myelitis to softening consequent upon vascular occlusion, in which inflammation plays no part, unless it is some inflammatory process in connection with the walls of the bloodvessels which tends to thrombosis and later softening. Douglas Singer also refers the majority of cases of myelitis to primary thrombosis.

It is well known but perhaps not thoroughly appreciated, that in cases of syphilis occlusion of some of the smaller spinal vessels produce sudden weakness and paralysis; in fact, sudden onset of paralysis is common in syphilitics. Spiller, in an article upon syphilitic acute anterior poliomyelitis due to thrombosis, emphasizes the importance of considering the rapid development of paralysis and says "spinal thrombosis is not a rare condition and is probably the cause of most of the apoplectiform palsies that occur in myelitis." In my case, syphilis, dislocation of vertebræ and trauma can all be excluded with certainty, yet a traumatic cause, if this expression is permissible, was present, that is to say compression. As has been already pointed out, compression of the spinal cord even when slight, can in itself cause œdema and inflammation with thickening of the bloodvessels within the cord, in other words, a fertile soil for thrombosis. Epidural inflammation and fungoid proliferations increase very gradually up to a certain point without evident disturbance in the functions of the cord unless it be pain; but when this point has been reached a very minute sudden increase may be sufficient to give signs of rapidly developing weakness or palsies, on the other hand, it is possible that it is just at this stage of the disease that thrombosis develops. Whether or not in my cases the initial palsies were caused by sudden increase of pressure with thrombosis, or to increased pressure without thrombosis, or to the changes which were found within the cord, is of course, problematical.

Raymond was inclined to look upon his case as one of hematomyelia, also Huber and Vorkarstner in discussing Martineck's case suggested the possibility of there having been a hemorrhage within the gray matter of the cord in addition to compression. Spontaneous hemorrhage in the spinal cord is exceedingly rare. Minor who has studied this question minutely, says that among all the cases which he has observed (other than Pott's disease) hemorrhage occurred only twice without preceding trauma. In an anatomical sense it is always difficult to make a sharp distinction between primary hemorrhage with subsequent myelitis from primary hemorrhagic myelitis and in many instances absolutely impossible.

In Cases I and II it was impossible to prove conclusively that thrombosis had taken place, nevertheless on account of marked thickening of the bloodvessels throughout the cross section of the

cord, together with extensive central softening and similarity of the onset of paralysis to cases of primary myelitis in which thrombosis has been proved, it seems more than probable that thrombosis may have occurred. At all events, instantaneous paralysis in Cases I and II and the more slowly developing paraplegia in Cases III and IV was the clinical expression of an intense myelitis and was beyond all doubt the direct result of compression of the spinal cord by means of tuberculous external pachymeningitis.

In determining the upper limits of a focal lesion causing compression of the cord, particularly when situated in the dorsal region, there is always more or less uncertainty. The most important single sign is the character and extent of sensory loss of function. Certain authors rely upon the level of hyperesthesia so frequently found just above the level of the total loss of sensation. In an article on spinal tumors Bailey maintains that the upper limits of incomplete loss of sensation is probably the most accurate guide in determining the exact level of the lesion. In two of my cases the lesions were too diffuse to draw accurate conclusions, but in Cases III and IV the limits of hypesthesia of the skin indicated quite accurately the segment of the cord which was involved.

The diagnosis of Pott's disease when deformity of the spine is present is generally easy, but, as Moussaud has pointed out, without this characteristic sign an accurate diagnosis may be exceedingly difficult or impossible. Fortunately, cases of this kind are uncommon, yet unmistakable evidence of caries is by no means always present. Nevertheless by a careful consideration of the clinical history, bearing in mind the similarity of the onset of paralysis in certain cases of Pott's disease with that of other form of myelitis particularly in syphilitics, and by use of x-ray examinations, tuberculin test, the Wassermann and Noguchi reactions, and lumbar puncture, in a certain number of cases at least, an accurate conclusion can be reached. If in a given case it can be proven that the bones of the vertebral column are not involved and the initial paralysis did not begin suddenly operation should be seriously considered. In such cases it is probable that the symptoms are caused by slowly increasing pressure upon the cord by a dry inflammatory exudate with a minimum amount of pus, or pus may be entirely absent as in Case III; therefore, if operation is done early and pressure removed recovery might be possible. Recovery does not seem to occur without operation. On the other hand, an apoplectiform onset of paralysis would indicate serious intraspinal lesions and operative interference might be of no advantage, and yet it is probable that in these cases also, compression is the primary etiological factor; if, therefore, it can be removed by operation, the injured cord will have better opportunity to recover its normal function, although in Case IV operation was of little benefit.

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THE PATHOLOGICAL FINDINGS IN THE PARATHYROIDS : IN A CASE OF INFANTILE TETANY. .

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IN the year 1880, the Swedish anatomist, Sandström, first described the parathyroids in man and also in the horse, cattle, cat, dog, and rabbit. In the same year, Nathan Weiss gave the first description of three cases of tetany after thyroidectomy; the condition was at that time called tetania strumipriva. Today, after thirty years, it is generally considered that such tetany, whether operative or experimental, is due not to the loss of the thyroid, but to the removal of the parathyroids (Vassale and Gencralli, Biedl, Pineles, Erdheim). In other words, the condition is not a tetania strumipriva, of the same origin as myxoedema and cachexia strumipriva, but a tetania *parathyreopriva*.

In regard to the so-called medical or spontaneous tetanies, however, it is at present still merely an hypothesis¹ that they are due to insufficiency of the parathyroid. Among such spontaneous tetanies

¹ For opposition to this theory see Berkeley, Forsyth, Kassowitz, and Thompson.

are included: The idiopathic workman's tetany, gastric tetany, tetany of pregnancy and lactation, of acute infectious diseases, and finally, children's tetany. The identity of all these clinical forms has not been established, but there are several symptoms common to them all, especially the electrical and mechanical irritability of the peripheral nerves. As regards their pathogenesis, there are some observations to indicate that the tetany of pregnancy and lactation may be due to parathyroid insufficiency (Vassale, Pineles, Erdheim, Adler and Thaler). For children's tetany, it has been the Viennese school (Escherich, Erdheim, and their pupil, Yanase) which has been most active in investigating the parathyroid in its relation to tetany and tetanoid conditions (spasmophilia). The recent view may be summarized about as follows: For all tetanies, operative, experimental, or spontaneous, a tetany toxin due to some disturbance in metabolism (possibly in calcium metabolism²) is presupposed. It is assumed to be a function of the parathyroid to neutralize such a tetany poison. If these glands through some functional or organic change are unable to neutralize this toxin, then the latter can act on the nervous system and produce the group of symptoms called tetany.

On looking for an anatomical basis for children's tetany, Escherich and his followers found hemorrhages or residua of hemorrhages in the parathyroid of children not uncommon, indeed in 33 out of 89 autopsies made by Yanase. These hemorrhages are thought to originate from intrauterine asphyxia, or some intrapartum injury.

Fifty of Yanase's 89 cases were tested as to their electrical irritability; none of the cases showing normal electrical reaction had hemorrhages in the parathyroid; all under one year showing electrical hyperexcitability presented evidences of hemorrhage. (After the lapse of one year all evidence of a prenatal hemorrhage of the parathyroids may be lost.) Among all Yanase's cases only 1 was a manifest tetany, 1 was merely tetanoid, 9 more were cases with convulsions. Below will be found a table of all the published cases of manifest tetany in children in which the parathyroids were examined; and in addition, a few important cases of allied conditions.

In America tetany in children is either less common than in certain parts of Europe or has escaped recognition. Perhaps with the more extended use of that essential guide to the diagnosis of infantile tetany and spasmophilia, the electrical examination, more cases will be discovered in the future. At any rate, up to the present, no pathological examination of the parathyroids of a fatal case of children's tetany has been published in this country.

² See for disturbances of calcium metabolism Erdheim, Hecker, Kassowitz, Leopold and Reuss, MacCallum and Voegtlin, Musser and Goodman, Parhon and Urech, Parhon, Dumitresco, and Nissipesco; also the views of Berkeley and Beebe, and Pexa.

TABLE OF PUBLISHED CASES OF MANIFEST TETANY IN CHILDREN IN WHICH THE PARATHYROIDS WERE EXAMINED.

Investigator.	Clinical diagnosis.	No. of cases.	Age.	Pathological condition of the parathyroid.
Erdheim	Tetany	3	3½, 5, 8 months, respectively	Hemorrhage
Escherich	Tetany in the course of tuberculous meningitis	1	7 years	Degeneration
Yanase	Tetany and meningitis	1	2½ years	Hemorrhage
	Tetanoid	1	3½ months	Hemorrhage
	"Krämpfe"	9	1 day to 5 months	8 cases hemorrhage
Königstein	Tetany	1	9 months	(1) Marked reaction with iodine and Best's glycogen method. (2) Increase in size
Harnett	Death with convulsions 12 hours after food-poisoning with diarrhoea, etc.	1	3 years	Congestion and minute traces of fat
Thiemich ³	Spasmophilia (not manifest tetany)	3	4, 11, 12 months, respectively	Negative
Forsyth	Tetany	1	Infant	Negative. Found only three parathyroids

The following is a report of such a case of manifest infantile tetany with the electrical examination and a description of the pathological findings of the four parathyroids:

Clinical History. B. J., aged eight months, was seen by Dr. Koplik February 23, 1909, in consultation with Dr. S. There were three other children in the family, all healthy and well. The patient was a well-nourished, bottle-fed infant. She had been well up to five days before the consultation, when without any known cause the child was taken with convulsions, which were repeated at short intervals. On the day of the consultation there had been one convulsion which had been controlled.

On examination, the child was easily startled in its crib, looked pale though well nourished, had very slight signs of a rachitic rosary, especially about the costochondral junction, no cranio-tabes, no marked enlargement of ends of the radii; there was no fever; fingers and hands were held in the typical accoucheur position, the forearm slightly flexed on the arm, the toes were strongly flexed, and any attempt to extend them painful. Examination otherwise was negative.

The diagnosis of tetany was made and the patient put under appropriate treatment.

The child was lost sight of until March 29, 1909, when it was admitted to the hospital with the following history:

The patient was born after an instrumental delivery; there were no paralyses, no convulsions. Infant was bottle fed from birth; its bowels at first were constipated, but now moved freely and were soft in consistency. No vomiting. No infectious diseases. About ten weeks ago patient was taken with fever and cough,

³ The cases of Thiemich have been criticised as not conclusive in several respects, apparently with justice; for example, in none of his cases did he find more than three glands.

which lasted for two weeks. Then it improved and was apparently well until six weeks ago.

The present illness began six weeks before admission to the hospital, when the child had convulsive attacks, which continued up to the time of admission. In these attacks the child at first seemed unable to get its breath; then had rigidity of the thumbs, which were flexed; the forearms were flexed; child became blue. These attacks lasted from two to five minutes; no cough. Between the attacks at times there were crowing sounds at the beginning of crying. Bowels continued normal.

The general condition on admission was excellent; the child's color was good; the head was well formed, the fontanelle open about one-half inch; no cranio-tabes; no rigidity of the neck; no MacEwen sign; the ears were negative; the pupils of the eyes were round and equal, reacted normally to light; there were no teeth; gums in excellent condition, tongue was clean; there was slight hypertrophy of the tonsils, thymus could not be percussed; there were no enlarged glands; the chest was well formed and symmetrical; there was a slight rachitic rosary as noted above; the heart presented nothing abnormal; the abdomen was normal, slightly tympanitic; the liver did not extend below the free border of the ribs; the spleen was not palpable.

March 30, 1909. When the child was seen by Dr. Koplik, the fingers and the arms were held in a typical tetany position, and the toes were held stiffly and were strongly flexed. The child cried just as on the first consultation, when attempts were made to straighten the toes. There was a Chvostek phenomenon, but the Trousseau phenomenon could not be elicited. The child had an anxious expression. It had had no convulsions since admission. On the same day the ulnar nerve was tested with the galvanic current to determine its electrical reactions. It was found that there were cathodal opening and closure contractions, and anodal opening and closure contractions to a current of less than three milliamperes. The anodal opening contraction was greater than the anodal closure contraction. (In other words, Erb's phenomenon of electrical irritability was established by the method of von Pirquet.)

April 1. The child showed contractures of the fingers and marked flexion of the toes; had had distinct attacks of laryngismus stridulus since it had been in the hospital, but no convulsions.

April 3. There had been frequent attacks of laryngismus stridulus, the infant was restless and had an anxious expression. The forearms were slightly flexed on the arms, fingers held in the tetany position and legs slightly flexed on the thighs. At 10.30 A.M. the nurse noticed that while crying the child suddenly became cyanosed and rigid. This lasted about two minutes, after which the baby appeared to be exhausted (tetany convulsion).

April 4. Child continued in very good general condition. In the previous twenty-four hours the typical tetany position had become very marked and then the fingers and toes had relaxed partly. A number of attacks of laryngismus stridulus had occurred with crying. About 4 P.M. the child suddenly became very pale, somewhat cyanotic, restless, apparently had a convulsion, and died in less than half a minute. Unfortunately the nurse gave no history as to whether the child had an attack of laryngismus just preceding this fatal seizure.

The patient was in the hospital seven days, and in that time the temperature ranged from 98.5° to 99.8°; the pulse was regular, 128 to 140 on admission, to 126 and 128 after admission. The child took its nourishment, from 33 ounces to 48 ounces daily, had one to three bowel movements of good color and consistency, and had a weight of 16 pounds 10 ounces.

On the first day of admission there were no attacks of laryngismus, but every subsequent day there were laryngismus attacks that were not alarming.

Pathological Findings. Autopsy 1774. B. J., aged eight and one-half months; died April 4, 1909, at 5.30 P.M.

Wound examination April 5, 1909, at 1 P.M.

As no autopsy was permitted, only a small incision in the neck was made. Through this, the larynx, trachea, thyroid, œsophagus, heart, and lungs were removed.

The larynx, œsophagus, and thyroid were negative. The thymus weighed 22 grams. Its length, after removal, was 7 cm.

The ductus arteriosus permitted the passage of the finest probe. The foramen ovale was closed. The heart was negative. The aorta was normal in width. The left lower lobe of the lung was adherent; otherwise negative.

Microscopic Examination. Thyroid: The interstitial connective tissue was very prominent. Thymus: Negative.

Parathyroid Glands. Macroscopic features: Four parathyroids (the normal number) were found; two of these were recognized on gross examination, the other two were discovered by dissection and microscopic examination of all the tissue in the neck which in any way resembled the parathyroid gland. Macroscopically the two glandules discovered with the naked eye were pale pinkish brown in color and nowhere showed any punctate elevations or irregularities of the surface which might have indicated hemorrhages.

Histological Features. The material was fixed in alcohol, embedded in paraffin, and serial sections 5 microns thick were cut and stained, most of them with hematoxylin; some with eosin-hematoxylin for colloid and oxyphil cells; some with ferrocyanide of potassium and hydrochloric acid for hemosiderin; and some with Gram-Weigert's stain for bacteria.

The histological features may be divided into: (1) Such as are normally found in infantile parathyroids; and (2) such as are unusual or pathological and might in some way account for or be associated with the tetany.

The parenchyma of each of the four parathyroids as may be seen in the plates, consisted entirely of the so-called principal cells, that is, of polyhedral, epithelial cells with clear or very faintly stained cytoplasm, and with a round or oval, sharply-defined, deeply-stained nucleus. In many parts of the glandules these cells were grouped in a compact mass as is usual in an infant parathyroid, and in many other parts the cells were arranged in strands or columns. The columns, one to eight cells deep, were separated from one another by vascularized connective tissue. The cytoplasm of most of the epithelial cells was either not stained at all or very faintly stained by means of eosin and hematoxylin. In some other of the principal cells the cytoplasm had a pink non-homogeneous appearance when stained with eosin. The cell membrane of the principal cells was sharp and well defined. The nuclei were comparatively large, deeply stained, and stood out prominently with sharp, round or oval outlines. The nucleoli and chromatin were well stained. The chromatin was granular and in the form of a network. In only one instance were the epithelial cells arranged in the shape of an acinus, with a central clear "vesicle." In several places the valves, first described by Yanase for the parathyroid glands, were found in the larger veins (Figs. 1 and 2). The connective tissue was moderately increased. No oxyphil cells, no colloid material, no fat cells, no bacteria and no hemosiderin were found. The bloodvessels were moderately congested. There were small hemorrhages in and underneath the capsule, but these might so easily have been the result of handling that they ought hardly be mentioned in this description. Similarly there were areas in which the cells were crowded together apparently because of the pressure of the microtome knife.

In parathyroid (I) there was a ring of round cells encircling one capillary. In parathyroid (II) along one border of fifteen successive sections there was a crescentic area of small round-cell infiltration (Fig. 3). These cells were about twenty-six rows deep and the area occupied about one-twelfth of the periphery of the glandule. In part, these round cells were separated from the epithelial cells by a few strands of connective tissue; in part, the round cells impinged directly upon the parenchyma cells. The nuclei of some of the round cells showed karyorrhexis. Beyond these fifteen sections this round-celled area could no longer be traced. In one gland in particular the perivascular lymph channels were undoubtedly dilated and filled with a granular coagulum (Fig. 4). In this same gland the most striking lesions of our sections were found. These were (Figs. 5 and 6) certain irregular areas occurring near

FIG. 1



FIG. 2



FIG. 1 ($\times 200$) and FIG. 2 ($\times 312$) show each a valve in a vein. All the figures are of sections of the parathyroid gland showing the principal cells (with their deeply-stained nuclei) arranged compactly as is typical for the infant parathyroid and separated into groups and columns by a vascularized connective tissue.

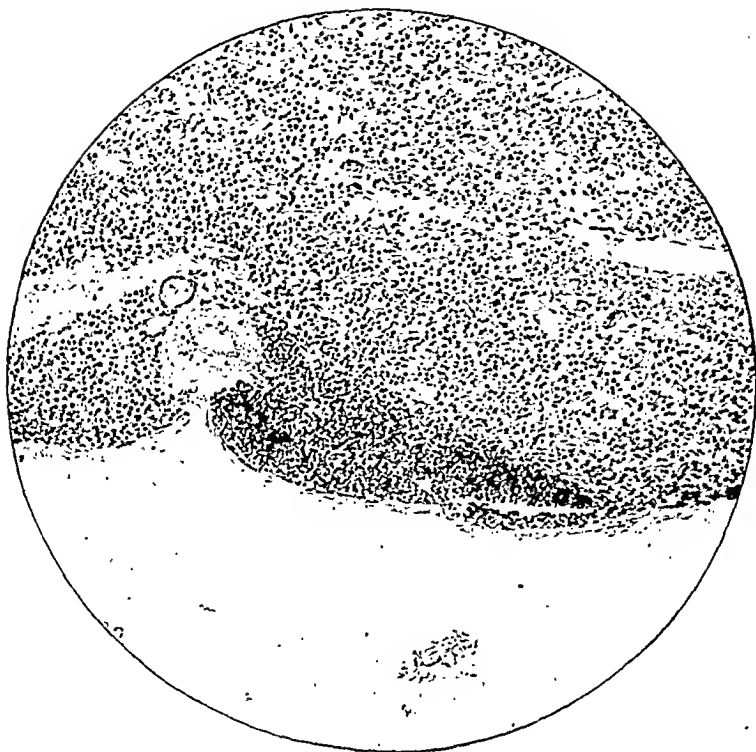


FIG. 3.—In the parathyroid along the border is an area of small round-cell infiltration. $\times 136$.

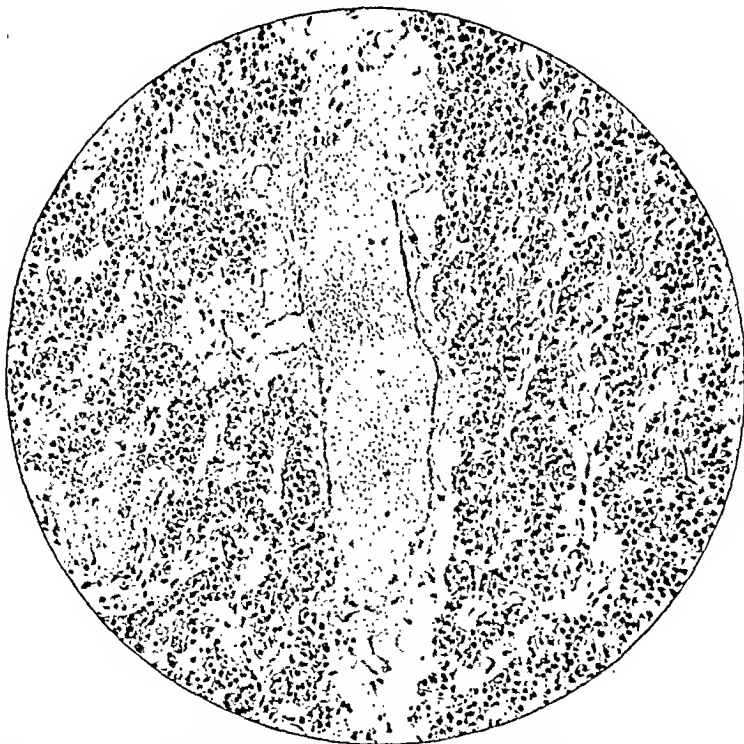


FIG. 4.—All along the right-hand border of the large vessel is a somewhat sinuous clear channel, a dilated perivascular lymph channel filled with a granular coagulum. Similar dilated lymph channels are seen distributed throughout the section. $\times 200$.

the larger bloodvessels and filled with the same granular material as the perivascular lymph channels. These areas were irregularly rounded or oval, triangular or crescentic in outline, the longest axis about one-fifth of the diameter of the parathyroid. They occurred more frequently at the periphery but sometimes also near the centre of the glandule. In some sections there were two, in some only one, in some no such regions; in one instance an area could be traced by means of its shape and location through sixteen successive sections of 5 microns each. Such an area presented the picture of a clear region, containing a finely granular



FIG. 5.—Shows an irregular clear area a little above and to the left of the centre. This is filled with the same granular material as is the perivascular lymph channel seen in Fig. 4—interpreted as a ruptured lymph space. $\times 100$.

coagulum with some entirely clear spaces and some detached nuclei and epithelial cells, but with no bacteria and with no red blood cells or pigment. In a few places, a longitudinal section of a capillary could be seen at the edge of the area or traversing it, but never communicating directly with its granular contents. The margins of these regions consisted chiefly of epithelial cells but also in part of bands or strands of connective tissue. The cells of the border projected into the area in the shape of little peninsulas and islets every here and there, and in the neighborhood of the margin seemed crowded together in anastomosing columns separated by narrow clear channels. Such clear channels appeared

to be the extensions of the clear spaces into the surrounding tissue breaking up the compact structure into strands.

Interpretation. Although only four parathyroids were found, and this is the usual number, it is possible that accessory and aberrant glandules escaped detection inasmuch as we did not make serial sections of the whole region in which the parathyroids may occur. In general these parathyroids presented the typical infantile structure with no signs of activity such as are indicated in older subjects by the presence of granular protoplasm, of oxyphil cells, and of acini with colloid. The increase in connective tissue and

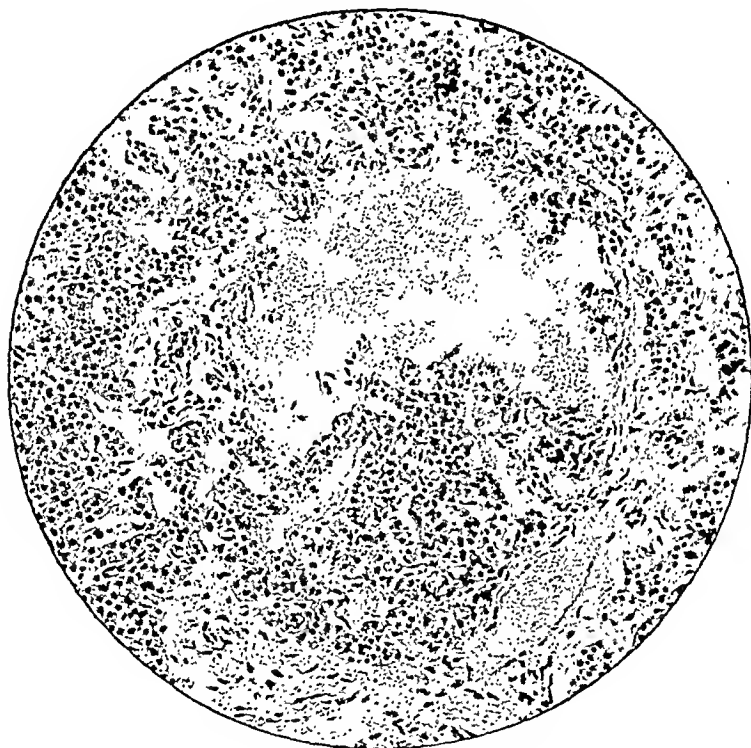


FIG. 6.—The irregular clear area of Fig. 5 much enlarged. It contains a finely granular coagulum with some entirely clear spaces and some detached nuclei and epithelial cells. It extends in the shape of clear channels into the mass of epithelial cells and connective tissue strands surrounding it. $\times 200$.

the congestion are common in parathyroid glands. As to the valves in the veins of the glandules, Yanase considers them a fortunate provision to compensate for the thin walls and great tendency to hemorrhages of the bloodvessels. Yanase found these valves only accidentally and has as yet made no study of their physiological or pathological significance. The round-cell infiltration had evidently no relation to the tetany inasmuch as it was only found in two relatively circumscribed regions. It should be noted that Yanase found numerous round-celled infiltrations in all four parathyroids in a case of pernicious anemia, and Guizzetti inflam-

matory foci of lymphocytes in the parathyroids in two cases of tetanus in adults. The areas which contained the same granular material as the dilated perivascular lymph channels and which occurred in their immediate vicinity are, in our opinion, *ruptured dilated lymph spaces*, or possibly regions of œdema. They were not lined with endothelial cells, but it is known that such lymph spaces bordered by parenchyma cells occur in the liver. These areas were found in the course of a painstaking search for hemorrhages such as have been described by Escherich, Erdheim, and Yanase, and are perhaps the most important pathological finding in the parathyroid glands of our case. We have seen one reference in the literature to similar appearances, but these occurred in two cases of tetanus, not of tetany. Guizzetti describes an extensive œdema and associated lymphatic stasis in one of the four parathyroids from a case of tetanus in a boy, aged eight years. In another case of tetanus in an adult, he found a somewhat similar granular substance around the bloodvessels and also infiltrating the tissue and could not demonstrate that this substance was the residue of an old hemorrhage. As these lesions have not been described before in tetany, and as we found them in only one of the four parathyroids, we think it wiser not to express any opinion as to their significance at present. We do desire to call attention to them and to ask other observers to report whether this condition of lymph stasis or œdema in the parathyroid is a frequent occurrence or an accidental result from some such cause as convulsions.

A very careful search, of course, was made for hemorrhages, "cysts," phagocytes, and pigment, such as have been frequently observed in parathyroids by the Escherich school. None of these were present. In view of the present-day discussion, a negative morphological finding is significant.

If it is somewhat difficult to consider the extensive hemorrhages of Escherich and his school as predisposing causes of tetany, it is still more difficult to consider the less marked lesions described above in our case as important factors in the production of fatal tetany.

My thanks are due Dr. F. S. Mandlebaum, director of the Pathological Laboratory of the Mount Sinai Hospital, for his valuable criticism of this histological study, and to Dr. Koplik for his encouragement in the pursuit of this work.

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SARCOMA OF THE VAGINA.

A STATISTICAL STUDY OF 102 CASES, WITH THE REPORT OF A
 NEW CASE OF THE GRAPE-LIKE SARCOMA OF THE
 VAGINA IN AN INFANT.

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SARCOMA of the vagina is so rare an affection that the literature contains a total of 101 cases to which I add a new one, making 102 cases upon record. Its rarity and its fatality combine to make it an interesting affection, and when an attempt is made to review the literature of the subject so many features of interest present themselves that the matter becomes quite absorbing.

Sarcoma of the female organs of generation may be divided clinically into those arising from the vulva, from the vagina, from the vesicovaginal septum, from the rectovaginal septum, from the cervix uteri, from the corpus uteri, and from the ovary. In selecting the cases embraced in the statistics given in this paper the attempt has been made to include only those arising from the vagina itself, though in a few the tumors occurred so low down as to be vulvovaginal, and of others the reporters stated that the tumors arose from the vesicovaginal or rectovaginal septa, though their descriptions showed that the tumors corresponded perfectly with vaginal tumors.

The literature begins quite early, in fact, before the separation of the sarcoma and other tumors was made by the microscope, and it is only the opinion of the reviewer, and not absolute knowledge of the tumor tissue that enables him to decide what shall be or shall not be regarded as sarcomas. In working over the case reports a confusion arose through the different methods employed by earlier writers in referring the cases to individuals. Thus, when the literature was reviewed by a clinician he was prone to refer all his collected cases to the clinicians in whose experience

they arose; if, on the other hand, the cases were collected by a pathologist, no attention was paid to this point. The result has been that in a number of the former tabulations and analyses certain cases have been counted more than once. To overcome this difficulty, the method adopted in the present writing has been to credit each case to the author first publishing it regardless of his actual relation to the patient, and to verify every case by referring to the original writing.

Unfortunately the case reports are so commonly imperfect that none of the tabulations can be complete. Thus, the table showing the age incidence contains a confusion of the ages at which the tumor was first observed and the ages at which the patient died. Usually the duration of the case is so brief that not much error results in consequence, but in the case of children it may be important, as in one case in which the tumor is known to have been present at birth, though the child did not die of it until the sixth year.

It is extremely unfortunate that the desire to report a rare case so often leads to its publication before knowledge of it is perfected. The case appears at the clinic, is recognized as a rare affection, an ingenious operation is performed, and the patient recovers from it. The clinician then hastens to report the case and tell what has been done without waiting to learn what the final outcome was to be. The evils of this practice are well shown by the tabulation showing the "Fatality of the Different Histological Forms of Sarcoma Vaginæ Exclusive of Sarcoma Botryoides Vaginæ," where out of a total of 58 cases, the termination of the affection is unknown in 34. It is likewise unfortunate that histological examinations have not been made in all cases. The same table shows that no histological data are available in 14 of the cases.

Sarcoma of the vagina occurs at all ages. In our collection of 102 cases there is 1 case in which the tumor was congenital, and 1 that came to operation when eighty-two years of age. It is, however, most frequent in the first, fourth, and sixth decades of life. The occurrence of a special form of infantile sarcoma—sarcoma botryoides, the "grape-like sarcoma"—of which 32 cases are on record, makes it overwhelmingly more frequent in infancy than at any other time of life. Though to all appearances a clinical form of the disease, the sarcoma botryoides vaginæ is so well characterized that throughout most of the following tabulations the tumors have been separated into "miscellaneous" and "botryoides."

The first case of sarcoma botryoides seems to have been recorded by Guersant in 1854; it is, however, difficult to decide what may have been the nature of many other tumors recorded earlier or about the same time as "malignant polypi" of the vagina. A number of such cases were carefully reviewed but rejected and

the policy was adopted of following the example of the earlier compilers who all accept Guersant's case as the first to be reported.

The first careful pathological studies, with special reference to the histology of the tumor came from Kaschewarowa-Rudwena, who curiously enough was able to report two cases from her own clinic, and also observed one in a bitch. Though this tumor differs from the other forms of sarcoma in its clinical manifestations, being characterized by a peculiar papillary or polypoid form with numbers of cysts—the grape-like sarcoma of Pfannenstiel, being observed only in infancy and being highly malignant, it is not so well characterized in all cases as to leave no room for doubt as to its proper classification, and is so varied in histology as not to find a separate place for itself. This is well shown by reference to the table showing the "Histological Forms of Sarcoma Botryoides."

Leaving this peculiar form in a group by itself, we find the remaining sarcomas to form a miscellaneous group embracing nearly all of the histological varieties of sarcoma. The peculiar appearance—grape-like appearance—of sarcoma botryoides has led to much speculation upon its origin. The early age at which the tumor makes its appearance suggests that the tumor is congenital but there is only one case, that of Granicher in which it is certainly known that the tumor was present at birth. Naturally a tumor in such a situation as the vagina might escape observation until it had become of sufficient size to exert pressure symptoms, or as is more usual, until it protrudes from the vulva.

Ahlfeld believed that the peculiar papillary and polypoid character of sarcoma botryoides was sufficient evidence that the tumor arose from the papillæ so numerous in the vaginal wall during the fifth month of intra-uterine life, and believed that all of the tumors were congenital. In this view he was followed by Aubert. Hauser and Kolisko, on the other hand, believe that the tumors are best explained by Cohnheim's theory of "embryonal vestiges," and Kolisko gives the following facts in support of his view: (1) The distribution of the tumor does not correspond with that of the papillæ. (2) The tumors commonly arise from a broad base and as single growths. (3) The tumors of the bladder resulting from extension of the growth are commonly polypoid, though there are never villi in the normal bladder. (4) The recurrent tumors preserve the polypoid character. The occurrence of a warty vaginal mucosa such as is described by Soltmann and was found in one of Kolisko's own cases can be attributed to the greater ease with which the tumor spreads in the mucosa as contrasted with the subjacent muscular tissue. (5) The structure with its miscellany of round and spindle cells, giant cells, muscle cells, epithelial cells, and cartilage, is in favor of Cohnheim's theory. Still another view of the etiology of the tumor has been suggested by Pfannenstiel,

that is, that it arises from the endothelium of the blood and lymph capillaries.

The clinical course of the sarcoma botryoides is much the same in all cases. The tumor first calls attention to itself either by projecting through the vulvar orifice or through the occurrence of a bloody discharge from the vagina. In most cases the diagnosis of "vaginal polyp" is made and the growth excised or divulsed. In most cases the tumor quickly recurs, after which there may be a succession of operations or a radical operation. In one case in which the operation was so radical that the entire vagina, uterus, tubes, and ovaries were removed the little patient is said to have recovered. In all other cases the tumor recurred, became inoperable, distended the vagina so as to fill the pelvis, invaded the bladder and caused the death of the patient either through exhaustion or from uremic blood poisoning. In no case has the tumor given metastasis. It is a purely local progressively extending tumor.

When the reports of other infantile sarcomas are read we find that they parallel the clinical course of sarcoma botryoides except that they lack the grape-like appearances, are not polypoid and not cystic.

The clinical course of the adult sarcomas is in general much the same. Though coming more early to operation, they, with the exception of the more benign forms, tend to rapid recurrence, to infiltrate the bladder and to cause a fatal termination through interference with the urinary passages. In these cases metastasis is very rare; the disease is local.

The geographical distribution of the tumor though shown in one of the tables is of small interest. The tumor attracted most attention in Germany, has been made the subject of numerous communications, and it is safe to surmise that few cases have escaped publication in that country. This gives Germany an apparent preponderance of cases.

The chronological distribution though more accurate is subject to the error that arises from evanescent interest in the subject. My tabulation is based chiefly upon the date of publication, but is inaccurate, because when interest upon the subject was aroused, cases from years before were sometimes hurried into print. The table shows, however, that the sarcoma botryoides averages one case each year and eight months; the miscellaneous vaginal sarcomas, one case each year and six months.

Certain writings on the subject, of special merit both from the scientific and synoptical points of view, should receive mention. The best of these are:

Veit. *Handbuch der Gynäkologie*, 1897, i, 354.

Powers. *St. Bartholomew's Hospital Reports*, xxxi, 1895.

Kolisko. *Wiener klin. Wochenschrift*, 1889, pp. 109, 130, 159.

Williams. *Twentieth Century Practice of Medicine*, 1898, xvii, 530.

Jellett and Earl. *Trans. Royal Acad. of Med. of Ireland*, xxii, 1904.

A word should be said with reference to the sarcomas that arise from the vesicovaginal and rectovaginal septæ. Being more deeply situated than the vaginal mucosa from which the true vaginal sarcomas arise, their tendency is to invade the deeper tissues, fill up the pelvis and give metastases to the pelvic and abdominal lymphatics and not to confine themselves to the vagina and bladder.

Sarcoma Botryoides Vaginæ—New Case. F. E. was born March 22, 1908, of parents in whose family history and in whose personal histories there seemed to be nothing of interest so far as the present circumstances are concerned. They were already possessed of one healthy child, and since the death of the one whose case we are about to consider, have become the parents of another.

On July 6, 1908, Dr. Robert L. Pitfield, of Germantown, was called to see the child, then aged three and one-half months, and shown a small tumor first observed by the nurse two days before. Two days later, at his request, we saw the little patient together and carefully examined the tumor, which proved to be peculiar and interesting.



FIG. 1.—Photograph showing the tumor projecting from the vulva when the patient cried and made expulsive efforts. This photograph was made shortly before the patient's death by Dr. George E. Pfahler.

When the thighs of the baby were separated, the vulvar orifice gaped slightly and permitted a laterally compressed reddish body of small size and moist appearance to be seen (Fig. 1). When the labia were more widely separated for a better view of the formation, the child began to cry and make expulsive efforts which resulted in the descent through the vulvar orifice of an irregularly hemispherical tumor about 3 cm. in its greatest diameter that sprang from the posterior and left lateral walls of the vagina. It was red in color and at first sight appeared smooth. This appearance was later found to depend upon the presence of considerable mucus with which the surface was bathed, for when it was wiped off so that a more careful examination could be made, the growth

was found to be composed of a polypoid mass, the intervals between the polypi being filled with the secretion and so disguised. Upon the surface of the tumor a number of small, clear, amber-colored cysts were conspicuous when the secretion was wiped off. The largest of the cysts was about 0.5 cm. in diameter. They gave the growth much the appearance of a bunch of currants infiltrated with reddish-gray slime.

When the child ceased to cry the tumor again retracted into the vagina. Dr. Pitfield had already made the diagnosis of "grape-like sarcoma," which I confirmed, though we were uncertain whether the growth originated in the vagina where we saw it or whether it sprang from the cervix uteri.

A very unfavorable prognosis was at once rendered, with the recommendation that an operation be immediately arranged for.

Some days later the child was taken ill with enterocolitis, and as at that time it was very warm and sultry in Philadelphia, it was taken to Ocean City, N. J. Here the patient was treated by Dr. Howard Reed, and speedily convalesced from the summer complaint. Upon July 24, Dr. Reed was able to operate and removed as much of the tumor as was attached to the vaginal wall. This mass, which was sent to me in formaldehyde solution, formed the foundation of my studies of the histological character of the tumor.

The child improved rapidly after the operation, but the wound did not heal and the tumor recurred so rapidly that on August 28 it was necessary to perform a second excision. In ten days the tumor had again recurred and grew so rapidly that it soon filled the entire vagina. The patient was now seen in consultation by Professor W. E. Ashton, who declared the condition to be inoperable. It was, therefore, thought that the x-rays might hold out a chance of benefit and the little patient was taken for the purpose to Dr. George E. Pfahler who began with three treatments weekly. The early results appeared encouraging. After six treatments the tumor had diminished to one-third of its original size, and after ten treatments to about one-fourth. An inguinal enlargement entirely disappeared. The baby was, however, much troubled with the summer diarrhoea and became very feeble. Partly because of the patient's general condition, and partly because he was to leave the city for a short time, Dr. Pfahler discontinued the treatments for a month. During that time, in spite of progressive emaciation and continued diarrhoea, the tumor grew again to its original size.

The condition of the little patient in the meantime became very distressing because of increasing difficulty of micturition and defecation. This difficulty increased to such an extent that the violent expulsive efforts of the patient had to be supplemented by com-

pression of the lower part of the abdomen by the mother or nurse in order that a small quantity of urine or feces could be discharged.

These conditions persisted and increased. The child suffered almost continuously, slept scarcely at all, emaciated almost to a skeleton, and died December 8, 1908, aged eight and one-half months, the tumor having been known to exist for just five months.

Autopsy. December 9, 1908. The body is that of a much-emaciated female infant. Rigor mortis marked. Thorax, abdomen, and left arm livid. Occasional petechia upon the skin.

From the vaginal orifice there projects a pyriform, dark colored, necrotic mass measuring about 1.5 by 2 cm. This can be traced into the vagina to a broad attachment upon the left lateral and posterior walls. Upon the surface a few small opalescent cysts (?) can be seen.

The appearance of the tumor is now very different from that first noted in the living child. Its grayish-red color is now changed to a dark necrotic red-black; its polypoid character has disappeared and it forms a solid mass. The clear cysts, like currants, that formed a large part of the original growth are gone and in their place are a few cysts with semiopaque contents. In addition to the chief mass there are a few pinhead sized nodules on the right labium majus, and a nodule the size of a pea in the vestibule.

The body was opened by the usual incisions, the nervous system not being removed.

Thorax: Pericardium, normal. Pleuræ, normal. Heart, normal—moderator band in the left ventricle. Right lung, hypostatic congestion. Left lung, hypostatic congestion; scattered foci of atelectasis. Thoracic lymph nodes somewhat larger and redder than is usual in infancy but otherwise normal. No thoracic metastases.

Abdomen: Spleen, large, bluish-purple, mottled. Upon section congested but otherwise normal. A small supernumerary spleen in the gastrosplenic omentum. Adrenals, normal. Liver, normal. Bile ducts, normal. Gall-bladder, normal. Duodenum, normal. Stomach, dilated. Small intestine, enlargement of the lymph follicles. Large intestine, enlargement of the lymph follicles. Mesenteric lymph nodes, slightly enlarged and red like those of the thorax. No signs of abdominal metastases. Kidneys, hydronephrosis and dilated ureters on both sides. The kidney substance also showed a mild grade of parenchymatous degeneration.

Pelvis: The pelvic cavity is completely filled by a mass formed by adhesion of all of the viscera. The chief mass is found to be the tumor distending the vagina. This tumor is dark red, almost black in color and forms a mass measuring 4.5 cm. in length by 3 cm. in breadth. It springs by a broad attachment from the posterior and left lateral walls about 1.5 cm. from the cervico-vaginal junction. The growth is lobulated and its surface generally

warty but highly necrotic. The anterior vaginal wall is invaded in its central third by an aggregation of wart-like formations most of which are sessile, though some are pedunculated. The vaginal wall at the attachment of the tumor is considerably thickened, and appears to be infiltrated around the base of the neoplasm; the remainder is thin and attenuated. At no point has the tumor broken through the vaginal wall except at its base. The right anterior vaginal wall is attached to the bladder by easily dissected adhesions, but on the left side the walls of the two viscera are so infiltrated by the neoplasm as to form a continuous mass.

Upon opening the bladder its wall is found to be infiltrated; and a mass of neoplasm about 2 cm. in diameter springs from the left anterior wall, occupies the entire trigone, and projects into the interior. Through the centre of this mass there is a ragged opening which connects with the urethra below. The bladder contains about 75 c.c. of turbid urine. The tumor mass in the bladder is entirely different in appearance from the vaginal mass, being grayish-pink in color. It is devoid of the hemorrhagic character of the vaginal growth. It is soft and oedematous. The surface is smooth and the substance translucent.

The uterus is very small and is peculiarly divided by a transverse cicatricial band so that the cervix and corpus are almost separated one from the other. The corpus also has a peculiar angulation and twist in consequence of the pressure of the band. The uterus is adherent to the bladder anteriorly and to the rectum posteriorly. It is, however, easily dissected free and is in no way invaded by the tumor. The vaginal portion of the cervix is slightly eroded, but it and the uterine mucosa are free of warts or polyps.

The rectum is so compressed as to be like a ribbon in appearance. It is empty and is not invaded by the tumor.

Both ureters were dissected and traced from the bladder to the kidneys. Their dilatation and the hydronephrosis does not depend upon obstruction of their vesical orifices, but is due to the regurgitation of urine during the efforts made to expel the urine from the bladder.

The right ovary and tube are in fairly normal condition.

The left ovary and tube are caught in a mass of adhesions and were not found in the dissection.

The tumor grew by continuous extension and infiltration; there were no lymphatic metastases in the pelvis.

The terminal sufferings of the patient were made clear by the cystic mass that obstructed the urethra and caused the backward flow of the urine into the ureters and pelves of the kidneys, and by the distended vagina which compressed the rectum almost to complete obstruction.

Death was probably caused by uremic blood poisoning following the damage to the kidneys, though it could be sufficiently explained by the exhaustion of the little patient through efforts to overcome

the mechanical impediments to urination and defecation. No signs of anything in the right groin to correspond to the mass that disappeared under the use of the x-ray could be found.

The original appearance of the tumor, with its polypoid cysts, like a "bunch of currants," its malignancy, the age of the little patient, and the clinical course seem to leave no doubt that the case belonged to the rare neoplasms to which Pfannenstiel first applied the term "*grape-like sarcomas*," and which are now frequently known as *sarcoma botryoides vaginæ*.

Histological Examination of the Tumor. The first tissue subjected to microscopic examination was that removed at the first operation by Dr. Reed. It is, indeed, the only tissue whose study has been of much use. Undue eagerness to preserve the entire pelvic viscera for the museum caused us to neglect to secure fragments for histological study, and when it became desirable to do so it was too late, as the reagents to which they had been subjected had destroyed their cellular structure (Figs. 2, 3, and 4).

The portion studied, therefore, corresponds to that examined by Dr. Pitfield, and myself, at our consultation of July 8, 1908, and consists of an irregularly hemispherical fragment. The flattened surface being that through which the cutting instrument passed; the rounded surface that of the tumor itself. Examination of this fragment shows that although it was removed little more than two weeks after it had been examined *in situ* it had undergone some change. It appears less lobulated and no longer contained the numerous cysts. Such cysts as are present appear smaller, and after immersion in the formaldehyde quite inconspicuous.

The sections cut for examination with the microscope were made in a direction perpendicular to the surface and passed through the entire thickness of the excised fragment.

The surface was, in general, covered with the vaginal squamous epithelium. This was more or less densely infiltrated with leukocytes, by which it was more or less completely disorganized in scattered areas. The destruction of the epithelium was almost confined to the exposed surface; where it dipped down between the papillary formations it was fairly well preserved. The leukocytic invasion was most marked upon the surface but occasionally penetrated to a considerable depth into the tissue of the tumor proper.

The tumor tissue began immediately beneath the vaginal epithelium, and in many places the superficial portion of the growth was a confused aggregation of dissociated epithelium, leukocytes, cells of the tumor proper, and cells that may have belonged to the fibromuscular tissues of the vaginal wall.

The more superficial portion of the tumor tissue differed from its deeper portions in a peculiar wide separation of the cellular elements ascribable to oedema. This oedema seemed to reach its maximum at occasional foci near the surface which appear to correspond to the

cysts. If such were the case, one was much deceived, for the cystic appearance was striking. However, the microscopic study of the tissues revealed the presence of no true cysts. This explanation of

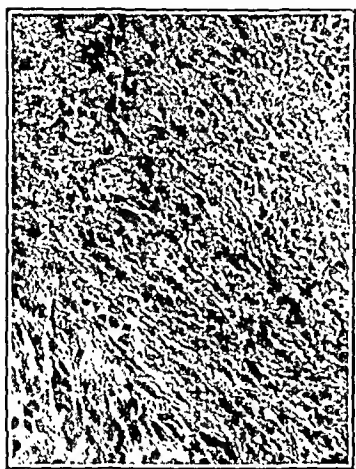


FIG. 2



FIG. 3

FIG. 2.—Photomicrograph showing the generally degenerated character of the tumor tissue, but still showing its structure to be composed of spindle-cells.

FIG. 3.—Photomicrograph of one of the oedematous areas of the tumor tissue.



FIG. 4.—Photomicrograph showing the surface of the tumor. The vaginal epithelium, by which the tumor is covered, is found to be fairly well preserved at this point, though it is separated and elevated at the centre, because of an extensive infiltration of leucocytes. Immediately below the epithelium the tumor tissue begins in a somewhat oedematous and miscellaneous collection of cells.

œdematous tumor villi and polypi simulating cysts is quite in keeping with the subsequent changes in its structure, for it appeared highly cystic when first seen, less so when Dr. Reed operated upon it, and scarcely at all so when it was finally examined at autopsy. In thus explaining the cystic appearances I am supported by the observation of Kolisko who, in speaking of the cyst-like formations in one of the tumors examined by him, says that "they were not actual spaces, but points at which the cells were widely separated from one another by fluid." It is a pity that we did not think to puncture one or two of them at the first examination, yet it is doubtful whether even such treatment would have made us sure of their nature, as the œdematous fluid would probably have leaked out much like the fluid from a punctured cyst.

The tissue of the tumor proper is almost entirely composed of spindle cells. They are somewhat irregular in shape and differ materially in different parts of the tumor. In what may be regarded as its "healthy" parts the cells are fairly regular in shape and form definite short spindles which lie side by side in fasciculi. Here and there one finds a strand of fibrillar tissue, but usually only in proximity to small bloodvessels. Here and there in the denser parts of the cellular growth small bloodvessels with only the endothelial coat may be found.

From such "healthy" and dense portions the tissue passes by imperceptible stages into the œdematous portions first described, where the cells are widely separated one from another and form a miscellany of spindle, stellate, clavate, and irregularly rounded cells. Among these are many leukocytes and not a few plasma cells. The nuclear structure is, in general, badly preserved. The formaldehyde fixation is imperfect, but only a small part of the appearance can be referred to it, as karyokinetic figures are numerous in the better preserved tissue areas, and though epithelial cells and leukocytes stain well, the nuclei of tumor cells in juxtaposition to them stain uniformly and palely. Again, in the poorly preserved portion of the tumor tissue and in the œdematous portions, though the nuclei of the leukocytes, cells of the bloodvessels, and those of a few of the tumor cells stain well, the generality of the tumor cells show more or less karyolysis and swelling to many times the normal size. Among the monstrous cells thus formed many have nuclei of giant size, and a few have several nuclei. These small giant cells are, however, too small and too few to merit much attention or affect the nomenclature of the tumor.

Although many sections were examined with care, no muscle cells other than could be accounted for by proximity to vessels, or be looked upon as remnants of the original vaginal tissue could be found. It was quite clear that neither muscle or cartilage were true components of the tumor.

The tumor, therefore, appears to be a simple *spindle-cell sarcoma* with localized foci of œdema and degeneration.

In the excised fragment only the epithelial coat of the vagina and the tumor tissue were present. It seemed clear that the tumor had grown in the mucosa, elevated the epithelium, and dissected it from the muscle.

Table Showing the Chronological Distribution of Cases of Sarcoma of the Vagina (not including Sarcoma Botryoides).

1867. 1 case.	Ahlfeld.	1894. 1 case.	Merutz.
1869. 1 case.	Meadows.	1895. 1 case.	Senn.
1869. 1 case.	Heckford. Infant.	1896. 2 cases.	Horn.
1872. 2 cases.	Spiegelberg.	1896. 1 case.	Rubeska.
1872. 2 cases.	Kaschewarowa-Rudwena.	1897. 1 case.	Amann.
1875. 1 case.	Fränkel.	1898. 1 case.	Morestin.
1875. 1 case.	Mann.	1898. 1 case.	Fränke.
1880. 1 case.	Biardi.	1899. 1 case.	Gebhardt.
1884. 1 case.	Simmons.	1899. 2 cases.	Jung.
1885. 1 case.	Mentzel.	1899. 1 case.	Smallwood-Savage.
1885. 1 case.	Underhill.	1899. 1 case.	Waldstein. Infant.
1885. 1 case.	Young.	1899. 1 case.	Strassmann. Infant.
1886. 1 case.	Gervis.	1900. 1 case.	Moovis.
1886. 1 case.	Handfield-Jones.	1900. 1 case.	Seitz.
1887. 1 case.	Parona.	1901. 1 case.	Piechand and Guyot. Infant.
1887. 1 case.	Spadaro.	1902. 1 case.	Macnaughton-Jones.
1888. 1 case.	Steinthal.	1903. 1 case.	Rashkes.
1889. 1 case.	Herzfeld.	1904. 1 case.	Jellett and Earl.
1889. 1 case.	von Rosthorn.	1904. 1 case.	Marullez. Infant.
1889. 1 case.	Marshall. Infant.	1905. 1 case.	Rollin.
1890. 1 case.	Odebrecht.	1905. 1 case.	Peyroche. Infant.
1891. 1 case.	Aglave and Mibian.	1906. 1 case.	Boldt.
1891. 1 case.	Ferrari.	1906. 1 case.	Potherat.
1891. 1 case.	Gow.	1907. 1 case.	Jellett.
1891. 1 case.	Hofmökke.	1907. 1 case.	Holmes. Infant.
1891. 1 case.	Kalustow.	1907. 1 case.	Amann. Infant.
1891. 1 case.	Wirtz.	1908. 1 case.	Moovis.
1892. 1 case.	Gatti.	1908. 1 case.	Rosenberger.
1892. 2 cases.	Oliver.	1908. 1 case.	Deck. Infant.
1892. 1 case.	Wirt.	1909. 1 case.	Favill.
1893. 1 case.	Tor Neumann.	1909. 1 case.	McLean.
1894. 1 case.	Klein.		
Total {		Adult	58
		Infantile	10

68 cases in 42 years.

Table Showing the Chronological Distribution of Cases of the Grape-like Form of Sarcoma of the Vagina or Sarcoma Botryoides Vaginæ.

1854. 1 case.	Gucrsant.	1896. 1 case.	Braun.
1874. 1 case.	Marsh.	1896. 1 case.	Hollander.
1880. 1 case.	Ahlfeld.	1900. 1 case.	Lea.
1880. 1 case.	Sänger.	1900. 1 case.	Starfinger.
1881. 1 case.	Soltmann.	1900. 1 case.	Brown.
1882. 1 case.	Hauser.	1902. 1 case.	Rabe.
1883. 1 case.	Babes.	1903. 1 case.	Wrede.
1883. 1 case.	Smith.	1904. 1 case.	Le Dentu.
1888. 2 cases.	Fricke.	1905. 1 case.	Aubert.
1888. 1 case.	Gränieher.	1907. 1 case.	Kelly and Noble.
1888. 1 case.	Kövrner.	1907. 1 case.	Rosenbach.
1888. 1 case.	Schustler.	1909. 1 case.	Schiller.
1888. 1 case.	Steinthal.	1910. 1 case.	Miller and Gurd.
1889. 3 cases.	Kolisko.	1910. 1 case.	Knoop.
1895. 2 cases.	Powers.	1911. 1 case.	McFarland.

Total: 34 cases in 57 years.

Table Showing the Anatomical Origin of Sarcoma Vaginæ, not Including Sarcoma Botryoides.

	Cases.
Vulvovaginal entrance	2
Entire circumference of the vagina	2
Anterior wall	20
Posterior wall	19
Right wall	2
Left wall	4
Vesicovaginal septum	1
Rectovaginal septum	1
Not stated	17
	<hr/>
	68

Table Showing the Anatomical Origin of Sarcoma Botryoides Vaginæ.

	Cases.
Vulvovaginal entrance	2
Whole vagina	2
Anterior wall	10
Posterior wall	4
Right wall	2
Left wall	4
Not stated	10
	<hr/>
	34

Table Showing the Geographical Distribution of the Reported Cases of Sarcoma Vaginæ, not Including Sarcoma Botryoides.

	Cases.
Germany	27
France	6
Italy	5
United States	5
British Isles	20
Austro-Hungary	4
Russia	1
Switzerland	1
	<hr/>
	69

Table Showing the Geographical Distribution of the Reported Cases of Sarcoma Botryoides Vaginæ.

	Cases.
Germany	21
Switzerland	1
United States	5
France	3
British Isles	4
	<hr/>
	34

Table Showing the Fatality of the Different Histological Forms of Sarcoma of the Vaginæ Exclusive of Sarcoma Botryoides Vaginæ.

Histological character of the tumor.	D.	Termination		Cases.
		R.	unknown.	
Round-cell sarcoma	0	1	8	9
Spindle-cell sarcoma (this includes Horn's case called alveolar spindle-cell sarcoma with much pigmentation)	5	3	9	17
Round- and spindle-cell sarcoma (this includes von Rosthorn's case in which Veit states that there were giant cells)	2	0	0	2
Myosarcoma (this includes all forms in which muscle cells were found)	0	0	2	2
Fibrosarcoma (this includes Ahlfeld's case called sarcoma fibrosum multo-et-fuso-cellulare telangiectoides diffusum)	1	2	0	3
Myxosarcoma	0	2	0	2
Melanosarcoma.	1	0	1	2
Giant-cell sarcoma.	0	0	1	1
Angiosarcoma (this includes Kalustow's case called sarcoma telangiectoides seu angiomatosum hemorrhagicum)	2	0	1	3
Endothelioma (this includes Klein's case called lymph - angio - endothelioma cavernosum hemorrhagicum)	0	0	3	3
Unknown	5	0	9	14
	<hr/> 16	<hr/> 8	<hr/> 34	<hr/> 58

Table Showing the Fatality of the Different Histological Forms of Sarcoma Botryoides Vaginæ.

Histological character of the tumor	D.	Termination		Cases.
		R.	unknown.	
Round-cell sarcoma	1	0	0	1
Spindle-cell sarcoma	3	0	1	4
Round- and spindle-cell sarcoma	5	1*	0	6
Myosarcoma (includes all cases in which muscle cells were found)	3	0	0	3
Myo-fibro-sarcoma.	1	0	0	1
Fibrosarcoma	2	0	1	3
Myxosarcoma	1	0	0	1
Unknown	10	1†	4	15
	<hr/> 26	<hr/> 2	<hr/> 6	<hr/> 34

* No return in 3 years.

† Was under observation only two months.

Table Showing Age Incidence, Histological Character, and Termination of Reported Cases of Grape-like Sarcoma of Infancy or Sarcoma Botryoides Vaginae.

Age of patient.	Cases.	Nature of the tumor.	Termination.
Not given	1	?	?
Congenital	1	?	Died.
3 months	1	Spindle-cell sarcoma	Died.
6 months	1	Spindle-cell sarcoma	Died (of bronchopneumonia).
6 months	1	Round- and spindle-cell sarcoma	Died.
7 months	1	Round- and spindle-cell sarcoma	Died.
8 months	1	?	Died.
9 months	1	?	No return in two months.
12 months	1	Myosarcoma	Died.
18 months	1	?	Died.
18 months	1	Myofibrosarcoma	Died.
18 months	1	Round- and spindle-cell sarcoma	Died.
18 months	1	Spindle-cell sarcoma	Died.
21 months	1	?	Died.
24 months	1	?	Died.
24 months	1	?	?
24 months	1	Myxosarcoma	Died.
28 months	1	Fibrosarcoma	Died.
28 months	1	Myosarcoma	Died.
30 months	1	Round- and spindle-cell sarcoma	Recovered (no return in 3 years).
30 months	1	?	Died.
30 months	1	?	Died.
30 months	1	Fibrosarcoma	?
30 months	1	?	Died.
32 months	1	?	?
36 months	1	Spindle-cell sarcoma	?
36 months	1	?	Died.
36 months	1	Small round-cell sarcoma	Died.
40 months	1	Fibrosarcoma	Died.
42 months	1	Myosarcoma	Died.
44 months	1	?	Died.
48 months	1	?	?
53 months	1	Round- and spindle-cell sarcoma	Died.
60 months	1	Round- and spindle-cell sarcoma	Died.

34

Table Showing Age Incidence, Variety, and Termination of Cases of Miscellaneous Sarcoma of the Vagina, not Including Sarcoma Botryoides.

Age of patient.	Cases.	Nature of tumor.	Termination.
8 months	1	Myxosarcoma	Died (of scarlatina while in the hospital).
10 months	1	?	Died.
11 months	1	Rhabdomyosarcoma	Died.
16 months	1	Perithelioma	Recovered.
17 months	1	Round-cell sarcoma	Died.
18 months	1	?	Died from peritonitis from accident to operation wound.
18 months	1	?	?
18 months	1	Endothelioma	Died.
24 months	1	Myosarcoma	Died.
31 months	1	?	Died.
14 years	1	Endothelioma	?
15 years	1	Sarcoma fibrosum multo-et fusocellulare telangiectodes hemorrhagium. (In our tables this is classed as fibrosarcoma.)	Died.
15 months	1	Spindle-cell sarcoma	Died.
15 years	1	Rhabdomyosarcoma	?
16 years	1	Round-cell sarcoma	Recovered.

Table Showing Age Incidence, Variety, and Termination of Cases of Miscellaneous Sarcoma of the Vagina, not Including Sarcoma Botyroides (Continued).

Age of patient.	Cases.	Nature of tumor.	Termination.
17 years	1	Spindle-cell sarcoma	Died.
17 years	1	Spindle-cell sarcoma	Died.
17 years	1	Spindle-cell sarcoma	?
19 years	1	?	Died.
23 years	1	Sarcoma telangiectoides seu angioma hemorrhagicum. (In our tables this is classed as angiosarcoma.)	Died.
25 years	1	Round-cell sarcoma	Died.
25 years	1	Round-cell sarcoma	?
28 years	1	?	?
28 years	1	Spindle-cell sarcoma	Discharged
30 years	1	Round-cell sarcoma	?
30 years	1	Myxosarcoma (myxoma?)	Recovered.
31 years	1	Melanotic spindle-cell sarcoma	Died.
32 years	1	Angiosarcoma	Died.
32 years	1	?	?
33 years	1	Small round-cell sarcoma	?
34 years	1	Spindle-cell sarcoma	?
34 years	1	?	Discharged in 6 weeks
34 years	1	Small round- and spindle-cell sarcoma	?
35 years	1	Fibrosarcoma	Recovered.
35 years	1	?	Died.
35 years	1	Spindle-cell sarcoma	Recovered.
37 years	1	Melanotic sarcoma	?
38 years	1	Spindle-cell sarcoma	?
39 years	1	Endothelioma	?
39 years	1	?	?
41 years	1	Spindle-cell sarcoma	Recovered
43 years	1	Round- and spindle-cell sarcoma with giant cells. (In our tables this is classed as a round- and spindle-cell sarcoma.)	?
44 years	1	Spindle-cell sarcoma	?
49 years	1	Spindle- and stellate-cell sarcoma with muscle cells. (In our tables this is classed as a myosarcoma.)	?
49 years	1	Alveolar spindle-cell sarcoma	Died.
50 years	1	Round- and spindle-cell sarcoma	Died.
51 years	1	?	Died.
54 years	1	Sarcoma, hypernephroma or lymphangioma hypertrophicum (In our tables we class this as histologically unknown.)	?
55 years	1	Angiosarcoma or endothelioma	Recurred
55 years	1	?	?
55 years	1	Spindle-cell sarcoma	Recovered
56 years	1	Lymphangio-endothelioma cavernosum hemorrhagicum. (In our tables we class this as endothelioma.)	?
58 years	1	?	Died.
58 years	1	Small round-cell sarcoma	?
60 years	1	Round- and oat-shaped-cell sarcoma	Died.
70 years	1	?	?
82 years	1	Spindle-cell sarcoma	Recovered.
Unknown	11		
		—	
		68	

Age Incidence of Sarcoma of the Vagina.

	Miscellaneous.	Botryoides.
First decade	10	34
Second decade	9	0
Third decade	5	0
Fourth decade	16	0
Fifth decade	5	0
Sixth decade	9	0
Seventh decade	1	0
Eighth decade	1	0
Ninth decade	1	0
	—	—
	57	34
“Young woman”	1	
“Old maid”	1	
Age not given	9	
	—	—
	68 miscellaneous	
	34 botryoides	
	—	—
	102 cases	

REPORTED CASES OF SARCOMA OF THE VAGINA.

I. INFANTILE. *Grape-like Sarcoma or Sarcoma Botryoides.*

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PROGNOSIS OF TUBERCULOUS LESIONS INVOLVING THE WHOLE OF OR MORE THAN ONE LOBE.¹

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THREE years ago Dr. Stanton called my attention to the fact that cases of tuberculosis of the lungs with large lesions (lesions involving an amount of tissue greater than the right upper lobe) usually did better when these lesions were on the left than on the right. As soon as the idea was mentioned I realized that I could recall more patients who were doing well with large lesions on the left than on the right, but I withheld full agreement until I made a further study. Further study confirmed this idea, and in the discussion of "The Heart in Tuberculosis," and of "The Primary Location and Development of Tuberculosis in the Lungs," before the meeting of the National Association in Washington, May, 1909, both Dr. Stanton and I mentioned the fact. It was not until this year, however, that I made a complete study of my private cases with this point in view.

Out of 1500 private cases of tuberculosis of the lungs I found only 67 with large lesions which I had seen over a sufficiently long time to make positive statements in regard to the exact involvement and the result. A study of these cases shows the following:

COMPARISON OF THE RESULTS IN CASES WITH LARGE LESIONS ON THE LEFT AND RIGHT SIDES.

Involvement.	Result.		
	Good.	Fair.	Bad.
Left upper lobe	1	2	3
Left lung	0	1	1
Left upper lobe and probably right apex	1	2	1
Left upper lobe and right apex	6	2	0
Left lower lobe and right apex	1	0	1
Left lung and right apex	2	2	0
Left upper and upper part of lower lobe and right upper lobe	2	0	0
Left lung and right upper lobe	1	0	2
Right upper and middle lobes	3	1	7
Right upper and upper part of lower lobe	0	0	2
Right upper and lower lobes	0	0	1
Right lung	0	0	4
Right upper lobe and possibly left apex	2	1	0
Right upper lobe and left apex	3	0	0
Right upper and upper part of middle lobe and possibly left apex	1	0	0
Right upper and middle lobes and possibly left apex	0	1	2
Right upper and upper half of left upper lobe	1	1	0
Right upper and middle lobes and upper half of left upper lobe	0	0	3
Right upper and upper part of lower lobes and upper half of left upper lobe	1	0	0
Right upper lobe and two-thirds of left upper lobe	0	2	0
Summary	<div> <div> <div>Large lesions on left</div> <div>14(45%)</div> </div> <div> <div>Large lesions on right</div> <div>11(31%)</div> </div> </div> <div> <div>9(29%)</div> <div>6(17%)</div> </div> <div> <div>8(26%)</div> <div>19(53%)</div> </div>		

¹ Read before the Sixth Annual Meeting of the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May, 1910

This table shows that even when we compare lesions of the right upper lobe with those of the left the latter are more favorable, though the comparison is not exactly just, since the left upper lobe is considerably larger than the right. If we omit as we should have done lesions confined to the right upper lobe, that is, lesions not affecting the right middle or lower lobe, the cases with large lesions on the right would stand as follows:

Involvement.	Result.		
	Good.	Fair.	Bad.
Large lesions on right	5(19%)	2(8%)	19(73%)

In addition, further study of the individual cases shows that there was no coincidence of character or environment favoring the left-sided cases, but, on the contrary, the surrounding circumstances favored the right-sided cases. Even the fact that in the cases with bad result we included no case that died of an accident like hemorrhage, pyothorax or pneumothorax favored the right-sided cases.

In the classification of the results, good result means that the patient is well and has been pursuing his ordinary occupation for a period of from two years to five years, except in two cases which have been working only one year; fair result means that the patient has been well for one year, but is unable to work; bad result means that the patient has died or is hopelessly sick in bed.

Taking everything into consideration, therefore, I have no hesitation in thinking that large left-sided lesions more frequently give good results than large right-sided ones.

Dr. Stanton's personal statement at the National Association meeting last year was as follows: "I have long been convinced that a large left-sided lesion offered a better prognosis than a large right-sided lesion. The kind of a case I refer to is familiar to every one working in tuberculosis. One rather frequently sees patients with complete left-sided involvement with rales over both lobes and the apex beat palpable and visible as far out as the left anterior axillary line. The right chest in these cases is usually much larger than the left and has a much greater amount of motion. Such patients often have a practically normal pulse rate and are able to do nearly the normal amount of work. While such a case as this is not uncommon, I have never been able to find a patient with the same amount of involvement on the right side who was able to get even a moderate amount of strength."

Dr. Stanton's original explanation of a possible cause for the better prognosis was: With large left-sided lesions the heart is drawn to the left, but this displacement is merely a drawing to the left and disturbs in no way the normal relation of the heart and vessels to each other; when, however, the heart is drawn to the right by a large right-sided lesion the relation of the heart to the vessels is disturbed by the heart turning on itself instead of merely

allowing itself to be drawn in a normal position. This turning over of the heart so that the apex, instead of pointing to the left, points to the right twists the vessels, with the consequence that extra work is put on the heart. This extra work on the already overworked heart is what changes the prognosis from favorable to unfavorable. This explanation appealed to both of us because we realized how much the heart has to do with making the prognosis favorable or unfavorable.

During the last year, however, in a careful study of the hearts of seventy-five autopsied cases dying of tuberculosis of the lungs, we found that the heart never did turn on itself, and when displaced to the right it appeared to be displaced, so far as we could see, in practically the same fashion as when it was displaced to the left. This explanation, therefore, fell to the ground.

A second explanation which I thought might mean something, and which I stated last year at the meeting of this Association, is that large right-sided lesions usually represent an acute or a sub-acute progression of the disease with little or no resistance, and large left-sided lesions are usually in cases which have advanced on account of causes not connected with the disease, like environment, etc., and which show that their susceptibility to tuberculosis is not great by the fact that they have already cured or practically cured a lesion at the right apex. The frequency of these cases is due to the frequency of the primary lesion at the right apex.

In the study last year of the primary location and development of tuberculosis I tried to show that clinical tuberculosis of the lungs has its primary seat more frequently at the top of the right than at the top of the left lung; that this lesion usually heals or almost heals, and in healing throws about itself a special resistance, so that if for any reason further dissemination occurs, it is usually implanted at the apex of the opposite lung. In exceptional cases the individual is too susceptible or the lesion too virulent to admit of healing, and the process extends acutely throughout the whole or a large part of the upper lobe, or even of the lung on the first side. In other exceptional cases, after half healing at the apex the resistance of the individual disappears, the half-healed lesion breaks down, and continues to advance on the same side. In the first or usual way of development the prognosis is better than in either of the latter ways.

Moreover, this explains some of the discrepancies we have found, for although, as a rule, large left-sided lesions give a good prognosis, there are exceptions to this rule, as is very evident in a study of the table, which are not to be explained by the mere extent of the lesion.

In addition, further study of the table shows that the cases which gave the best results were those in which there was a large lesion on the left with chronic involvement of the right apex, or a large lesion on the right with chronic involvement of the left apex; while

the cases that gave the majority of bad results were cases with large lesions on the left without any lesion on the right, or cases with large lesions on the right without any lesion on the left.

Rearranging the table on page 589, we find a large lesion in one lung with none in the other in 26 cases, a large lesion in one lung and a doubtful lesion in the other in 11, and a large lesion in one lung and a small or medium sized lesion in the other in 30. Omitting the middle category, since the lesions are not positive, we have:

COMPARISON OF THE RESULTS IN CASES WITH A LARGE LESION IN ONE LUNG ONLY, AND A LARGE LESION IN ONE LUNG WITH A SMALL OR MEDIUM SIZED LESION IN THE OTHER.

Involvement.	Result.		
	Good.	Fair.	Bad.
Large lesion in one lung only	4(15%)	4(15%)	18(60%)
Large lesion in one lung, small or medium-sized lesion in other lung	17(57%)	7(23%)	6(20%)

There have been several pathological papers written to show that the primary lesion of tuberculosis in the lungs is as frequently at the top of the left lung as at the top of the right, among which one of the most recent and most conclusive is that of Adami and McCrae before the International Congress on Tuberculosis in Washington in 1908.

Out of 1000 cases autopsied, 417 showed evidence of past or present tuberculosis in some organ. Of these 417, 100 cases showed small areas of calcification or fibrosis in the lungs; in other words, small healed lesions; 72 cases showed small areas of caseation, but without recent activity; in other words, latent disease. In these 172 cured, or practically cured cases the lesions were slightly more frequently on the left than on the right. The writers do not state the frequency with which the different sides were involved by the more advanced lesions; in other words, their statistics are strictly limited to pathological lesions.

In this paper, however, I am considering clinical lesions. I would be unwilling to consider a case with a cured tuberculous wart on his finger as a cured case of clinical tuberculosis, and in like manner, am unwilling to consider a spontaneously cured single tubercle in the lung as a cured case of clinical tuberculosis. As the situation of the tuberculous wart depends not on the greater susceptibility of the right or left hand, but on the accident of inoculation, so I believe such tubercles as they describe in the lungs may be due to the same cause. Despite the pathological findings, therefore, I believe that clinical tuberculosis, that is, tuberculosis in cases with some susceptibility, begins more commonly at the top of the right lung.

In addition, a study of the progression of tuberculosis of the lungs on autopsies at the Phipps Institute showed that in the cases in which it was possible to judge the progression, the progression commonly corresponded to what I have pointed out as the most fatal clinically; in other words, the majority of the cases showed progression practically throughout one side before the other was involved. I do not wish to emphasize this fact, however, since this study of the progression from a pathological standpoint was not very satisfactory on account of the number of cases in which the progression could not be judged.

In the discussion of this subject last year the idea was suggested that the cases of large involvement which did so well might have been cases with thickened pleura instead of actual lung involvement. In answer to this I would say that practically all the cases presented in this paper, especially those with very large lesions, were examined not only by me, but by others (Dr. Flick, Dr. Stanton, etc.), and after the last seven years' experience with autopsies in which we have seen our clinical diagnosis practically constantly confirmed I am not willing to grant even the possibility of this.

In addition, I might add that I have studied the cases from the standpoint of cavity formation and other special features in connection with both the disease itself and the circumstances of the patient, like age, sex, environment, etc., and have found nothing further to account for the better result in the left-sided cases.

CONCLUSIONS. 1. Lesions involving the whole of one lobe of the left lung usually give better results than lesions of the same size in the right lung. One reason for this appears to be that the large lesion on the left more frequently represents the secondary development in a somewhat resistant case.

2. Lesions involving an amount of lung tissue the size of the left upper lobe give a better prognosis when the opposite side shows a chronic healed lesion.

REVIEWS.

THE EXPECTATION OF LIFE OF THE CONSUMPTIVE AFTER SANATORIUM TREATMENT. By N. D. BARDSWELL, M.D., M.R.C.P., F.R.S., Medical Superintendent of the King Edward VII Sanatorium. Pp. 130. Edinburgh, Glasgow, and London: Henry Frowde and Hodder & Stoughton, 1910.

THE book comprises statistical details and the life histories in brief of 241 patients. From the beginning of the author's sanatorium work he attempted, year by year, to keep in touch with the physical condition of the discharged patients, and in this he has met with a fair degree of success. As to the stage of disease, the classification employed is that adopted by the National Association, while the manner of tabulating after-results is along the lines adopted by the Germans. Some of the tables show the physical condition of the patients, the effects of different occupations, and their capacity for work at the end of four to seven years after discharge. The life histories are classified according to incipient, moderately advanced and far advanced stages. From one who has had considerable experience in the sanatorium treatment of tuberculosis, the book is of interest particularly in noting the "post-sanatorium life" of the patients and its effects. The author epitomizes the results of his efforts, which are obviously painstaking, with the statement that he is unable on account of insufficient evidence to estimate the average length of "post-sanatorium life." The book presents the subject, which has received but little attention in England and America, in a systematic and attractive manner.

W. T. C.

AN ANATOMICAL AND SURGICAL STUDY OF FRACTURES OF THE LOWER END OF THE HUMERUS. By ASTLEY P. C. ASHHURST, M.D., Prosector of Applied Anatomy in the University of Pennsylvania, Philadelphia. Pp. 158; 150 illustrations. Philadelphia: Lea & Febiger, 1910.

In this, the Samuel D. Gross Prize Essay of the Philadelphia Academy of Surgery for 1910, the author has made a careful analysis of fifty-six cases of fracture of the lower end of the humerus which have come under his care in the various dispensary services in which he has been working. They are illustrated by a large number

of good skiagrams, plates, and diagrams. No claim is made for originality, either in diagnosis or treatment, beyond the careful and systematic examination of his cases, which is so characteristic of Dr. Ashhurst's work. His classification of these injuries is based on good anatomical and morphological lines. In the directions which are so clearly outlined for the treatment of these injuries, namely, the position of hyperflexion which was routinely employed because it is the one position in which the fragments are retained accurately in place without the aid of pads, splints, etc., the results obtained will be in marked contrast to the usual methods now pursued; so that the average practitioner may approach the treatment of injuries of this character with the expectation of obtaining a good functional result in a large percentage of the cases treated. The work evidences the greatest care and accuracy, and is invaluable to the practising surgeon and teacher. It is also an inspiration to young men just entering upon their careers, who have perhaps only a dispensary service, for it shows them what valuable material is to be found in every clinic, requiring only the careful noting, study, and classification so exemplified in these fifty-six cases of injury of the lower end of the humerus collected by the author. The general arrangement of the cuts and plates reflect great credit on the publishers, and we commend the work most heartily to all persons interested in this class of injuries.

R. H. H.

PULMONARY TUBERCULOSIS AND SANATORIUM TREATMENT. By C. MUTHU, M.D., M.R.C.S., L.R.C.P., Physieian to Mendip Hills Sanatorium, etc. Pp. 201; 10 illustrations. London: Baillière, Tindall & Cox, 1910. New York: William Wood & Co., 1910.

THE author has prepared the volume in three parts, which deal with the scientific, the sanatorial and the social aspects of tuberculosis. Verses of several well known poets have been used in a pertinent manner to introduce many of the chapters. Though the subject comprising the so-called scientific section is taken up in a systematic, clear, and comprehensive style, there is much for adverse criticism. The author unduly emphasizes the importance of heredity. He states that the symptoms of tuberculosis may spontaneously arise from the evolution of the common forms of bacilli (also pneumococci) in the tissue without direct infection with the tubercle bacillus—an extraordinary statement. This he designates as "spontaneous tuberculosis." The term "contagious" is not employed with its usual significance. In Part II every aspect of sanatorium treatment is considered, including inhalation and electrical treatment. However, one questions the potency of formaldehyde in curing tuberculosis through hardening of the mucous

membranes. But little reference is made to drug therapy, aside from inhalants, while considerable emphasis is made in a lengthy section upon walking and respiratory exercises, both of which are objectionable from the quantitative standpoint. The nucleus of Part III is made up of suggestions relative to social reforms, and these are stated so clearly, forcefully, and intelligently that one enthuses in approbation of his plans. As a whole, the book shows in a well systematized, although in some instances not scientifically commendable, text the subject of tuberculosis and the author's detailed experience in sanatorium treatment. W. T. C.

THE PRINCIPLES OF GYNECOLOGY. By W. BLAIR BELL, B.S., M.D., Assistant Gynecological Surgeon to the Royal Infirmary, Liverpool. Pp. 551; 363 illustrations. London: Longmans, Green & Co., 1910.

"Of the making of books there is no end," and it is a great pity. By far the larger number could be well spared. Only rarely does a book appear above the horizon of the reviewer which can justify its existence. This being the case, it will readily be realized how pleasurable has been the work of the reviewer in this instance, as this book may be justly said to be one of the best for the use of students and general practitioners as yet published. The first three chapters are devoted to the evolution and development of the female generative organs, together with their anatomy and physiology. Chapter IV is concerned with history-taking and methods of examination, while Chapters V to VIII inclusive deal with the congenital and acquired derangements of the normal anatomical and physiological conditions of the pelvic organs. In the last mentioned chapter, when discussing certain disorders of menstruation, the author allows his enthusiasm to run away with his judgment to some degree in the advocacy of the calcium therapy; while there is no doubt that the work done in recent years upon the physiology of the ductless glands is pregnant with possibilities, there is still too much that is uncertain and too much completely hidden to allow of quite as much definiteness of opinion as is expressed by the author. The whole subject, however, is intensely interesting and the enthusiasm is easily forgiven.

The chapters immediately succeeding are concerned with the disorders of the normal physiological conditions as related to conception, with the infective and parasitic diseases of the genital tract and with neoplasms, both innocent and malignant, together with the allied morbid conditions. Chapter XV deals with the preparation of a patient for operation and her subsequent care. The only criticism of an adverse nature is that it would be well

to drop ealomel from the postoperative routine. Chapter XVI, comprising 71 pages, is a synoptical description of the main principles of gynecological operative procedures, together with some details of their technique. In the main there is nothing but commendation for this portion of the work, though it seems a pity that ventrosuspension is not alluded to and that a few interrupted silkworm-gut sutures are not advocated in the layer method of abdominal closure.

The book closes with an appendix of five pages upon electrotherapeutics as applied to gynecology, and one of ten pages in which the causes of certain cardinal symptoms are classified, as, for instance, hemorrhage, amenorrhœa, etc. Throughout the whole volume the author has in an almost unexampled manner linked the cognate subjects of gynecology and obstetrics, thus enhancing the value of the work many times. We can only end as we began, by saying that the book is one of the best that we have ever read upon this subject.

W. R. N.

NEPHROCOLOPTOSIS. A DESCRIPTION OF THE NEPHROCOLIC LIGAMENT AND ITS ACTION IN THE CAUSATION OF NEPHROPTOSIS, WITH THE TECHNIQUE OF THE OPERATION OF NEPHROCOLOPEXY, IN WHICH THE NEPHROCOLIC LIGAMENT IS UTILIZED TO IMMOBILIZE BOTH KIDNEY AND BOWEL. By H. W. LONGYEAR, M.D., Professor of Gynecology and Abdominal Surgery in the Detroit Post-graduate Medical School. St. Louis: C. V. Mosby Company, 1910.

THE author looks upon the nephrocolic ligament as the principal etiological factor in the production of nephroptosis; further, because of the action of this ligament, he believes that nephroptosis must invariably be the result of eoloptosis, except when due to trauma, and, consequently, he has coined the term nephrocoloptosis to indicate the eo-relation existing between these two conditions. He describes the nephrocolic ligament and gives directions for its demonstration upon the cadaver. The anatomy and pathology of the kidneys and adjacent viscera are considered in so far as they bear upon the subject under discussion. The primary etiological factor in the production of nephroptosis is relaxation or absence of the hepatocolic ligament, which permits the cecum and ascending colon to sag and to exert traction on the kidney through the nephrocolic ligament. Nephrocoloptosis manifests itself chiefly through gastric and colonic symptoms, which the author details clearly and accurately. With the exception of Dietl's crises, the kidney participates but little in the clinical picture. The skiagraph is invaluable in the diagnosis of eoloptosis. In his preface the author

asserts that very few general practitioners know how to examine for nephroptosis, and the reader anticipates with interest the description of a new method; the procedures described are generally known and employed. Treatment may be prophylactic, medical, and surgical. The author's method of suspending the colon and kidney by means of the nephrocolic ligament is described and excellent illustrations demonstrate the various steps of the operation. It is difficult to comprehend how this operation can produce such remarkable results as are reported in fifty-six cases. Were the chief manifestations referable to the kidneys, one might understand how suspension by this method could give relief. When one considers, however, that the symptoms detailed are largely due to ptosis and angulation of the colon, malformations which the operation does not correct, one is forced to the conclusion that the author has read his results through the eyes of an enthusiast. F. E. K.

KLINISCHE UND ANATOMISCHE BEITRÄGE ZUR LEHRE VOM UTERUS-MYOM. Von DR. MED. ANTON GARKISH. Berlin: S. Karger, 1910.

THIS monograph of 148 pages comprises an analytical study of 399 cases treated in the German Gynecological Clinic at Prague from 1900 to 1908. The first portion is devoted to the various clinical manifestations of myomata, which the author discusses in a thorough and interesting manner. Statistics are at times burdensome but impossible of elimination in a work of this nature. After defining the indications and contraindications for the various operative procedures, he tabulates the postoperative morbidity and concludes that spinal anesthesia and short confinement in bed are potent factors in reducing the number of pulmonary complications and thromboses during convalescence. The subsequent examination of 225 patients demonstrates the value of conserving one or both ovaries, especially in women under forty years of age. With the exception of a brief presentation of prevailing views concerning the histological aspects of myomata, including their degenerations and associated alterations in the endometrium, tubes, and ovaries, the second portion is devoted to the enumeration of a long series of detailed case histories, operations, and histological findings—a fault so frequently encountered in such monographs. While this contribution adds nothing new to our knowledge of myomata, it represents painstaking efforts in accurately summarizing the data presented by a large gynecological clinic, and is of value in that it confirms existing ideas regarding one of the most important pathological changes found in the uterus. F. E. K.

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF
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An Early Sign of Aortic Sclerosis.—N. G. KUKOVIEROFF (*Russki Vrach*, No. 51, 1910) reports a new sign of beginning arteriosclerosis of the aorta which has not hitherto been noted. Out of more than 2000 cases he was able to diagnosticate early sclerosis in 164 patients not presenting the ordinary physical signs of the lesion. The diagnosis was corroborated by the later history of the cases and by radioscopy. The signs consisted of a systolic bruit heard over the course of the beginning aorta and over the sternum about the second and third costal cartilages when the arms are *raised* above the head. The bruit comes from the root of the aorta and is due to changes in vibrations of the blood column produced by the sclerotic changes and accentuated by the position of the arms. This sign has the same significance as the ordinary systolic murmur heard in patients with sclerosis of the aorta, but it is of *importance* because it is present—as in the 164 cases reported—in patients who do not give other evidence of the lesion, and is an *early* sign. It is, however, carefully to be differentiated from the venous hum or cardio-respiratory murmurs sometimes heard in this region.

Autoserotherapy in Serofibrinous Pleurisy.—N. T. CHIGAYIEFF (*Russki Vrach*, 1910. No. 51) reports 56 cases in which this treatment was essayed. Of these, 6 were failures. In 8 the results were unsatisfactory. In 42 the absorption of the effusion was complete and rapid. In 15 of the 42, only one injection was required; in the rest from two to four injections. The author comes to the conclusion that subcutaneous auto-inoculation with the patient's exudate, whether in tuberculous or non-tuberculous cases, is quite harmless and causes neither local nor constitutional disturbances of any importance. There may follow a slight rise in temperature, but this amounts to no more

than a fraction of a degree. In patients with pulmonary tuberculosis, no changes in the tuberculous process are noted. In the majority of cases absorption of the effusion begins very soon after the subcutaneous injection. The pleurisy is healed in from two to three weeks, sometimes in one week—although it had been of long standing. The earlier the injections are made the sooner is the pleurisy cured. The absorption of the effusion is marked by increased diuresis; subjective symptoms are in all cases improved.

A New Test for Cancer of the Stomach and the Tryptophan Test.—OPPENHEIMER (*Deutsch. Archiv. f. klin. Med.*, 1910, ci, 293) relates his experience with the glycytryptophan test of Neubauer and Fischer for the detection of cancer of the stomach. His results were, on the whole, very satisfactory. One interesting case with gummata of the left lobe of the liver but no cancer (operation) is recorded, in which both tryptophan and acetic acid test (vide infra) were positive. Oppenheimer has discovered a new test which gives practically the same results as the tryptophan test. The procedure is the following: Forty minutes after an Ewald breakfast, the stomach is emptied and the contents filtered. To the clear filtrate one adds 3 per cent. acetic acid cautiously, a drop at a time. In case the reaction is positive, a turbidity or cloud appears which vanishes only after considerable acetic acid or a little hydrochloric acid is added. Dilution with one to five volumes of distilled water causes the cloud to remain. The only source of error is mucus which also gives a cloud with acetic acid; but this cloud is unaffected by the addition of a few drops of HCl and does not occur in high dilution of the gastric contents. If the gastric filtrate is so turbid that dilution with an equal quantity of distilled water does not clear it the acetic acid test cannot be employed. Slow filtration through a wet, folded filter usually yields a clear filtrate. Oppenheimer has not determined the cause of the reaction. In all cases where the tryptophan test was positive, the acetic acid test was also given (except where turbidity of the filtrate precluded its employment), including the case of hepatic gummata. The test may be applied to vomitus, and blood and pancreatic juice are not disturbing factors as in the glycytryptophan test.

Lipemia in Diabetes.—KLEMPERER (*Deut. med. Woch.*, 1910, xxxvi, 2373) has investigated the lipemia which so frequently accompanies acidosis in diabetes. From observations on a fairly extensive material he has shown that lipemia causes large quantities of cholesterol and lecithin to appear in the blood plasma. These substances are not derived from the subcutaneous fat. There is no diminished fat destruction (consumption) on the part of the organism. The increase in blood lipoids Klemperer attributes to the heightened cell metabolism in severe diabetes. Cell katabolism throws the lipoids into the blood stream from which they are removed by the anabolic activity of the body cells. Thus the lipemia results from the mobilization of lipoids in the body.

Intrathoracic Struma.—KREUZFUHS (*Munch. med. Woch.*, 1911, lviii, 23) finds intrathoracic struma not infrequently in Vienna. Of 1040 Röntgenologic examinations (both thoracic and abdominal) in

the last seventeen months, 1.25 per cent. were pure substernal strumas. In five other cases a process from a cervical goitre extended beneath the sternum. The symptoms of intrathoracic struma are largely the result of pressure. Dyspnea was the most constant complaint and was often independent of exertion. "Dyspnea in the absence of disease of the lungs or circulatory system should always suggest substernal struma." Palpitation of the heart is frequent but is nearly always associated with the shortness of breath. Dysphagia is commoner than might be supposed. It is seldom so severe as in cancer of the thyroid, and regurgitation is rare. Hoarseness from paralysis of the recurrent laryngeal, stridor from tracheal stenosis, and cough are less frequent, though important, symptoms of substernal struma. Likewise dullness under the sternum, dilatation of the veins in the neck and on the upper anterior chest wall, redness and puffiness of the face, and cyanosis of the lips are found in a small proportion of the cases. Inequality of the radial pulses is a rare symptom. In the literature a few other symptoms are reported, such as unilateral exophthalmos with unilateral sluggishness of the pupil, prominence of a clavicle or the sternum, and fixation of the larynx. Though perhaps not common, a low position of the larynx is very important and appears to be pathognomonic. It must be remembered that with cervical struma it happens at times that the gland extends beneath the manubrium sterni to a sufficient extent to cause all the symptoms enumerated above.

Intravenous and Subcutaneous Administration of Dextrose.—KAUSCH (*Deut. med. Woch.*, 1911, xxxvii, 8) has had gratifying results from subcutaneous or intravenous administration of glucose in patients unable to retain food in the stomach or rectum. No complications or sequelæ have occurred in more than 40 cases. The sugar is dissolved in 0.85 per cent. sodium chloride solution, filtered, and boiled to sterilize it. For subcutaneous use, Kausch employs 1000 cc. of a 2 per cent. sugar solution. The percentage can be increased gradually to 5. Intravenous injections of 1000 c.c. of 5 to 7 per cent. glucose are well borne. If an 8 or 10 per cent. glucose solution is used, 2 to 10 per cent. of the sugar injected is excreted in the urine. In some cases the author has used two intravenous injections of one liter daily. The subcutaneous infusion is no more painful than plain physiological salt solution. While the author's experience has been confined to surgical cases, he recommends that this method of feeding be extended.

Generalized Syphilitic Infection of Rabbits.—UHLENHUTH and MULZER (*Deut. med. Woch.*, 1911, xxxvii, 51) have made important studies upon experimental lues in rabbits, the result of which they summarize as follows: They have succeeded repeatedly in producing a generalized syphilitic infection in rabbits. Young animals, especially when infected by the intracardiac method described by the writers, have yielded the most constant results. The experimental disease is characteristic. Nasal and caudal tumors are observed which are similar to human gummata histologically. The emaciation, paronychia, and papulo-ulcerative syphilides all remind one of hereditary lues in man. In all of these lesions the spirochetæ are demonstrable. Furthermore, the authors have succeeded in obtaining living *Spirochetæ pallidæ*

from the circulating blood in experimental syphilis. The results should be valuable in the study of chemotherapy, in the study of hereditary tues, of parasymphilitic nervous affections, immunity, etc. By repeated passage of the spirochetæ through successive animals, it has been possible to increase the virulence of the organisms.

The Bearing of Old and New Facts Upon Our Conceptions of Cardiovascular Disease—In the past the heart received first attention and the vessels were considered last in importance. HARE (*Interstate Med. Jour.*, 1911, xviii, 277) now believes that the pendulum has begun to swing in the opposite direction and the careful study of the vessels will give as much information as is obtained by direct examination of the heart. Following along the line pursued in a recent report in the *Therapeutic Gazette* (June, 1910) on the value of studying the blood pressure in pneumonia for the purpose of determining the state of the heart muscle and the need for stimulation or cardiac support, he emphasizes the great importance of the use of the sphygmomanometer. A daily record of the patient's circulatory state is possible, and any tendency to circulatory failure can be discovered early and promptly combated. He calls attention to an important observation made by Gibson: "A pressure appreciably below normal in pneumonia is invariably of evil omen, and any considerable fall bodes disaster. When the arterial pressure, expressed in millimeters of mercury, does not fall below the pulse rate expressed in beats per minute, the fact may be taken as an excellent augury; while the converse is equally true." In all cases of pneumonia in which the blood pressure fell to the pulse rate, or below it, active stimulation is instituted. When the blood pressure bore a normal ratio to the pulse rate, and the heart sounds were satisfactory, no drugs were resorted to. Regarding the use of drugs, much caution should be exercised in the giving of nitrites and they should only be used in cases where the pressure is so high that there is fear that the heart will become exhausted in trying to drive the blood through the narrow blood paths. He emphasizes two important facts in the use of digitalis. This drug powerfully stimulates the vagi and so primarily slows the auricles and indirectly the ventricles. The auricular walls themselves are very little stimulated if at all, but the ventricular walls are powerfully stimulated and are caused to beat more forcibly and if the ventricular walls are cut off from the vagus influence by injury to the bundle of His, they also contract more frequently under digitalis than before the drug is given. The use of digitalis in a case of partial heart block may precipitate a fatal attack of the Stokes-Adams syndrome, while in cases in which there is complete destruction of His' bundle, or complete heart block, digitalis may be advantageous, since the ventricles are no longer in the slightest degree under control of the auricles and are increased in power and in frequency of contraction and are able to supply the body with greater volume of blood. This fact is well borne out by the experimental work of von Tabora. In conditions in which the cardiac conductivity is decreased, there seems to be little doubt that digitalis still further impairs it. In the case of a patient suffering from circulatory failure due to mitral stenosis, after carefully weighing the import of the heart sounds, instruments of precision should be used to determine if possible whether there

is any delay in the transmission of the contraction impulse over His' bundle. If such a delay exists, great care should be exercised in the use of digitalis, and if the drug is given at all, the dose must be so small as to produce a very gradual effect, one which will not consist in decreasing auricular contraction through vagal stimulation, but gently reestablish general cardiac power.

On Chylous and Pseudochylous Ascites. — Through an extensive search of the literature, WALLIS and SCHOLLBERG (*Quarterly Jour. of Med.*, 1910, Part I, iii, 301; 1911, part II, iv, 153) have traced 171 cases of chylous and pseudochylous ascites. This number includes 3 cases coming under their own personal observation and in which they made exhaustive chemical examination of the fluid obtained through tapping. In addition they have given synopses of 60 cases of chylous and pseudo-chylous hydrothorax, and 8 cases of milky pericardial effusion recorded in the literature. Their conclusions are as follows: Milky ascitic fluid may be recognized in two main types—chylous and pseudochylous. The milky appearance of the latter is not due to free lecithin, fat, or a mucinoid substance, but to a lecithin globulin complex, which is held in suspension by the inorganic salts present in the fluid. By dialysis these inorganic salts may be removed, the lecithin globulin complex precipitated and the opalescence of the ascitic fluid disappears. The marked resistance of the fluid to putrefaction is due to the presence of lecithin. The prognosis in cases of milky ascites is grave and the mortality reaches 70.4 per cent. in cases of pseudochylous ascites, and 66 per cent. in chylous ascites. No specific morbid anatomy lesion may be said to be characteristic of milky ascites. In order to differentiate with certainty between the two types of milky ascites, a complete chemical and physical examination is necessary, and the results obtained seem to have a direct bearing on the question of the chemical physiology of the blood serum, particularly with regard to the serum proteins and carbohydrates present. In comparing the two main groups of milky ascites we find the following most distinctive features: Chylous ascites tend to accumulate more rapidly and the emulsification present is less perfect. The degree of opalescence is more or less constant and does not show the variations of the pseudochylous fluid. The odor of the fluid corresponds to the odor of the food ingested, while the pseudo-chylous ascitic fluid is odorless. Few cellular elements are found in the chylous fluid, and both types contain fine fat globules. On standing, chylous fluid exhibits a distinct creamy layer. This may or may not be present in the pseudochylous fluid, and in the latter the opalescence is not affected, and frequently a sediment settles out. The specific gravity of chylous fluid is usually higher than the pseudochylous type, and generally exceeds 1.012. The depression of the freezing point approximates that of chyle, while that of the pseudochylous more nearly corresponds to the figures of blood serum. The total solids vary considerably but are usually greater than 4 per cent. for chylous fluids and rarely exceed 2 per cent. for pseudochylous. Globulin occurs only in traces in chylous ascites and the total protein content generally exceeds 3 per cent. The protein constituents in pseudochylous fluids vary between 1 and 3 gram per cent. Mucinoid substances are absent in chylous fluids, but sometimes are found present in the pseudochylous

groups. The fat content in chylous fluid is generally high, and the fat corresponds to the fat contained in the food. In the pseudochylous fluid the fat content is low and may be present in traces; its melting point and chemical composition proves it to be pathological fat. Cholesterolin is the invariable characteristic lipine to be found in the chylous fluid and lecithin occurs in traces. Lecithin exists in larger quantities in the pseudochylous type. No evidence of the lipine globulin combination is to be found in chylous ascites. Such a combination is present in the pseudochylous fluid, and is the cause for the opalescence and the resistance to putrefaction. The salts and the organic substances approximate the value found for chyle from the thoracic duct. While in the case of pseudochylous fluid they correspond more closely to the lymph and serous fluid.

S U R G E R Y.

UNDER THE CHARGE OF

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The Origin and Treatment of Ischemic Contracture and Gangrene.—BARDENHEUER (*Deut. Ztschr. f. Chir.*, 1910, cviii, 44) says that the contracture is due to the ischemia, but more especially to the venous stasis dependent upon it and to the influence of the carbonic acid on the nuclei of the muscle fibers. The ischemic infiltration is induced by the obstruction of the venous blood rich in carbonic acid. The stasis and ischemic infiltration result from the wounding of the arteries, chiefly by an intima rupture of the main vessels. However slight it may be, as from the application of a tourniquet, this suffices to produce ischemic contracture. The importance of the intima rupture depends upon the size of the wounded vessel. The more central the intima rupture, the greater is the stasis and the danger of gangrene, as well as the disturbance of nerve conduction from the venous stasis along the nerves. Ischemic contracture occurs also after partial or total tearing of the whole thickness of the arterial wall, although this cause is a very rare one, at least of isolated ischemic contractures. It is generally followed by total gangrene or the formation of a traumatic aneurysm. Ischemic myositis may develop after a simple contusion of the arterial and venous walls with small simultaneous injury to the collateral vessels, the bed of the vessels, and a secondary infiltration, traumatic and inflammatory in character. The arterial circulation need not be interrupted. Usually one speaks of ischemia of the flexors, but when the stasis is severe the extensors may also be involved. The pathogenesis of ischemic infiltration (myositis) is as follows: In consequence

of a central interference of the blood current, usually as a result of a severe wounding of the vessel bed, as from a supracondylar fracture, there develops a peripheral stasis of the limb, first in the venous trunks below the elbow. The stasis extends from here to the adjacent muscles, the flexors, and in the vessels even to the capillaries and arteries, so that the arterial current becomes more and more slowed. The ischemic myositis always lies below the central cause and below the joint, lying next below. The blood obstructed in the capillaries destroys the nuclei in the capillary walls, so that they become permeable to the blood serum which exudes, and the stasis and tension in the muscles are further increased. The diagnosis of an ischemic myositis depends upon the recognition of a central cause of the disturbance of the blood current, recognition of the acute ischemic myositis, the ischemic contracture, and the accompanying nerve affections. The recognition of the central cause is very important for the preventive treatment, as no constricting bandage should be employed in the presence of such a condition. Upon the first development of the acute myositis, the infiltration and tension at the site of the central cause must be relieved. It may be necessary to make incisions in the fascia and muscles for this purpose. After fibrous degeneration of the muscles appears, one of several operations may be performed to lengthen the contracted muscles or shorten the bones.

Calculous Anuria in a Case of Single Kidney, Treated and Cured by Ureteral Catheterism.—ANDRE (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 132) says that the classic treatment of calculus anuria is nephrectomy, practised as soon after the beginning of the symptoms as possible. Those who are in the habit of employing the ureteral catheter have the opportunity of trying this method before resorting to the knife. Cures by it have been reported. If it is not successful, operation can then be carried out without exposing the patient to the danger of much delay, as the passing of the catheter takes only a short time. A man, aged forty-two years, entered the hospital, September 22, 1910, because he had not been able to pass urine for forty-eight hours. Six years before he had suffered from renal colic for the first time, and two months later had another attack, in which he passed a calculus about the size of a pea. For three days preceding the beginning of the anuria in this attack he had passed discolored and turbid urine, when he was taken with severe pains in the hypogastric and iliac regions, especially on the left side. On September 20 he urinated only once. From then until his entrance into the hospital he did not pass any urine and his pain was persistent. A catheter introduced into the bladder did not evacuate any urine. The left ureter was catheterized immediately, the catheter penetrating easily into the renal pelvis without encountering any obstacle, and from it escaped urine with some force, indicating that it had been retained in the pelvis under some tension. This continued until 70 grams had escaped, then drop by drop. The ureteral sound was left in place and the patient carried back to bed. In the first twenty-four hours the total quantity passed by the sound was 1800 grams. During the following twenty-four hours it was 2600 grams. On the other hand, the patient passed spontaneously 1850 grams on the first day and 500

grams on the second day. After forty-eight hours the catheter was removed and the patient urinated easily and abundantly. The kidney which had been blocked manifested a hyperactive secretion. On September 29 a careful and prolonged cystoscopic examination failed to find the orifice of the right ureter, and it was concluded that there was probably no right kidney. Shortly afterward the patient was discharged well. He did not pass a calculus, and a skiagraph taken of the left kidney was negative. There was probably a small calculus present. It is the small calculi which usually provoke anuria.

A New Gastrostomy Operation.—LAFARO (*Deut. Ztschr. f. Chir.*, 1911, cviii, 307) makes an incision in the abdominal wall in the median line, from the tip of the xyphoid cartilage downward three or four inches. The left hand is then introduced into the wound and the abdominal wall on the left side grasped between the middle finger and thumb. In this way the left rectus muscle is located. With a long tenotome an opening is made through the substance of the left rectus from the wound surface to emerge on the skin surface a few centimeters within the outer border of the rectus. This opening is widened by cutting upward and downward and dividing the rectus into two equal layers, an anterior and a posterior. The size of this passageway should correspond to that of the portion of the stomach which is to be drawn through. This portion of the stomach is then drawn through with a suitable forceps and its base sewed to the posterior edge of the median end of the passageway with three catgut sutures. The opposite surface of this base is then sutured to the peritoneum and rectus on the opposite side of the median wound. The deep edges of the upper and lower portions of the median wound are then brought together by sutures. The end of the projecting portion of the stomach is now conducted through the tunnel made for it in the rectus muscle and skin and its apex is fastened to the skin edges of the small lateral external opening. The large median wound is then closed over the projecting portion of stomach by two layers of sutures, one for the fascia and the other for the skin. Finally, the emerging end of the stomach is opened and its edges sutured to the skin. This operation provides a strong, permanent sphincter for the gastrostomy opening and makes it continent.

Ligation of the Vein in Portal Thrombosis from Appendicitis.—SPRENGEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 33) reports a case similar to that in which Wilms ligated the veins passing from the ileocecal region to the liver for the relief of symptoms of liver sepsis following the evacuation of a periappendicular abscess. Sprengel had operated for a perforative appendicitis. The symptoms of a portal vein phlebitis were apparent nine days later, and four days after this, or thirteen days after the first operation, he did a second operation. The drainage wound was thoroughly irrigated, cleansed, and closed by suture. A transverse incision was then made to the left, beginning about the middle of the original wound and passing through the right rectus and into the left rectus. The intestines were carefully packed off. Pressure on the cecum opened up the old focus of inflammation. A mesentery for the cecum and ascending colon could not be made out, so that the

veins leading from the cecum were exposed with great difficulty. The posterior peritoneum was rich in fat, so that the exposure was made still more difficult. The mesentery of the lower ileum and the peritoneum of the ileocecal angle with the vessels lying behind it were ligated obliquely in several bundles. The transverse incision in the abdominal wall was sutured and abundant drainage provided. The chills which had been present before the second operation were after it repeated several times and they then ceased. The fear of a diffuse peritonitis was not realized and the abdomen remained soft and painless. There developed, however, a fecal fistula, with irregular temperature, slight jaundice, and the clinical picture of general sepsis, from which the patient died three weeks after the second operation. The autopsy showed, together with the localized focus of infection and the fecal fistula of the lower end of the ileum, a thrombophlebitis of the superior and inferior mesenteric veins, portal thrombosis with extension into the finest branches of the portal vein, numerous abscesses in the liver, enlargement of the spleen, and myocarditis.

Making a New Circulation for an Obstructed Circulation in the Abdomen and Lower Extremities.—LANZ (*Zentralbl. f. Chir.*, 1911, xxxviii, 3) says that the cases of elephantiasis which occur in his practice result usually from repeated attacks of erysipelas, in which phlebitis and lymphangitis lead to an inflammatory obstruction of the lymph vessels or from the obstruction of the lymph due to the removal of lymph nodes by operation. In most of them a transitory oedema develops, but in some the lymph stasis becomes permanent and is accompanied by thickening of the subcutaneous tissue. In a troublesome case, after a trial of ten days elevation of the right leg without much success, Lanz made an incision on the outer side of the thigh in its whole length, dividing the fascia lata and exposing the bone behind the posterior edge of the vastus externus muscle. After separating the periosteum from the bone, three openings were made into the medulla, in the upper, middle, and lower thirds of the femur. Narrow strips of fascia lata were then excised, which were introduced into the bone openings, with the hope that along them a collateral circulation of the lymph would develop. The fascial wound was then closed by a suture and many small openings made in the fascia with scissors to favor the escape of the lymph. The skin wound was closed and a collodion dressing applied. The patient left the hospital a few weeks with the wound healed. A year later he reported for examination, when the wound was still healed. Three years after operation examination showed the following result: While before the operation he was compelled from time to time to stop work for three hours and lie down, immediately after the operation he began to improve, and at the present time he can work all day without difficulty. He was examined about four o'clock in the afternoon after working all day, and on inspection there was no important difference in the size of the two limbs. Lanz has had no further opportunity in the last five years to operate again in elephantiasis.

Operative Mobilization of the Upper Jaw in Cleft Palate.—CODIVILLA (*Zentralbl. f. Chir.*, 1911, xxxviii, 105) reports the case of a boy,

aged five years, with a double harelip and a cleft palate involving the hard and soft palate, which was so wide that the fissure in the alveolar process admitted easily two fingers. Without a preliminary operation on the skeleton, sufficient flaps could not be obtained from the cheeks to unite them in the median line except under very severe tension. The usual methods of closing the cleft in the bone could not be employed. While on the left side the bone appeared to have its normal direction and relations to the dental arch, on the right side the superior maxilla was displaced upward and outward, so that the buccal surface was somewhat cone-shaped, with its apex at the basilar bone. Codivilla concluded that the gap could be closed and the abnormal position of the superior maxilla corrected only by mobilization of the latter. A preliminary ligation of the external carotid was performed. Through a small incision in the cheek over the articulation between the superior maxilla and malar bones, this union was separated and the anterior wall of the former divided. On the buccal side the union between the maxilla and the pterygoid process was also divided. By strong pressure with the thumb the alveolar process could be brought close to the intermaxillary bone and thus the nasobuccal gap closed. The abnormal position of the maxilla was also corrected by force and fixed in its new position to the opposite bone by a metallic ligature. In the mouth the fixation was aided by a plate in the roof of the mouth fixed to the teeth on both sides. This apparatus was kept in place for six months without any considerable difficulty and was then removed. The bone was now firmly united and the correction of the deformity excellent. With the aid of a plastic operation on the cheek, the harelip was then closed. Codivilla says that this is the first case in which the maxillæ have been approximated by open operation in cleft palate. Several years after operation the correction of the deformity was still maintained and there was no disturbance in the growth of the teeth.

Anesthesia by the Intratracheal Insufflation of Air and Ether. A Description of the Technique of the Method and of a Portable Apparatus for Use in Man.—ELSBURG (*Annals of Surgery*, liii, 161) describes a portable apparatus for the employment of the Meltzer-Auer intratracheal method of inducing general anesthesia in man. In all but one of the cases the anesthesia was complete, the patients being quiet, their muscles relaxed, and the breathing quiet and superficial. In many but not in all of the patients the respiratory movements ceased altogether when the pressure of the air passing into the trachea was so raised that the manometer registered 30 to 40 mm., and apnoea ensued. If the tracheal tube is of the correct size and in proper position, the face of the patient will be of a pink color, with the veins of the forehead slightly prominent. The pulse is full, bounding, and regular. It is possible to keep a patient under primary anesthesia a long period of time if the proper percentage of ether is given with the air. Several of the patients had sensitive corneas during the operation, but they were relaxed and gave no evidence of pain. They were almost fully awake as soon as the insufflation was stopped. There is an entire absence of mucus rattling in the throat during the entire operation. None of the cases had any cough or expectoration at any time, and none had any pulmonary complication of even the mildest kind after the operation.

Uniformly there was no complaint of a feeling of discomfort in the region of the larynx after operation and there was no postoperative vomiting. About 30 patients have been anesthetized by this method, some for intrathoracic disease, many for abdominal or other affections. It has been found very useful in operations about the head and neck, as the anesthetist was never in the operative field or in the way of the operator or his assistants.

THERAPEUTICS.

UNDER THE CHARGE OF

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Salvarsan in Syphilis.—WEILER (*Münch. med. Woch.*, 1910, lvii, 2622) has treated 206 cases of syphilis with salvarsan. Forty of these have been under observation for some time, and a recurrence has been observed in 14. Three of these cases have shown symptoms referable to the cranial nerves. Weiler says that it is impossible to interpret these as results of the medication or as syphilitic manifestations. In another case hemorrhagic nephritis developed a few weeks after the injection. Weiler believes that salvarsan has a more rapid action than the usual antisiphilitic remedies in most cases, but that as yet its permanent results are not fully established.

Experimental Studies of the Lethal Dose of Salvarsan in Acid Solution.—HERING (*Münch. med. Woch.*, 1910, lvii, 2621) relates his experiments with the injection of salvarsan in dogs and rabbits. He found that the lethal dose of the acid solution in 0.5 per cent. strength was from 0.004 gram to 0.005 gram per kilo for rabbits and from 0.01 to 0.02 gram for dogs. This makes the lethal dose for a man weighing 150 pounds 0.315 gram if based upon the results in the rabbits, or 1.05 gram if based upon the lethal dose for dogs. Hering believes that the acid reaction is mainly responsible for the toxicity, as he found that the rabbits would survive twenty times the fatal dose and dogs ten times if the drug were given in an alkaline solution.

Atropine Cure in Ulcer of the Stomach, and other Indications for Atropine in Internal Medicine.—SCHICK (*Wiener. klin. Woch.*, 1910, xxiii, 1229) believes that good results are obtained by the use of atropine in the treatment of gastric ulcer. The subjective symptoms, especially pain, disappear quickly after beginning the treatment. Hyperæidity and hypersecretion were less quickly influenced. Pyloric stenosis due to cicatricial contraction was either not at all or only slightly influenced. Schick agrees with the view of Eissinger and Hess that many ulcer cases are dependent upon an increased vagus tone. This increased vagus tone stimulates the gastric secretion as well as the gastric mus-

culature, and can be diminished by a systematic use of atropine. He mentions a long list of conditions benefited by this drug. Among these are spastic constipation, bronchial asthma, excessive sweating, nervous hypersecretion, lead colic, membranous colitis, in certain cases of intestinal obstruction, in cardiospasm, in spasms in œsophageal carcinomata, in gallstone, and renal colic.

The Prevention of Typhoid Fever with Antityphoid Vaccine.—RUSSELL (*Boston Med. and Surg. Journ.*, 1911, clxiv) says that vaccination is a simple and harmless procedure and wherever used has reduced the incidence and mortality of typhoid. The immunization of every individual in the army is perfectly feasible, and it offers the greatest hope of freedom from this plague in the future. Antityphoid vaccine has long since passed the experimental stage. Since 1904, 60,000 men have been vaccinated in India, over 7000 in Southwest Africa, and over 14,000 in the United States. In no case has any harm followed its administration.

The New Preparation of Albumin, "Riba."—VON NOORDEN (*Berlin. klin. Woch.*, 1910, xlvii, 1919) reports that a new preparation of albumin has been perfected after a year's experiment. This is sold under the name "Riba." It is derived from fish and in composition consists principally of albumoses. The preparation is easily soluble in water and is well borne by the digestive tract, and because of its ease of absorption it is of great value in nutrient enemata. It has no unpleasant taste and may be combined with other articles of food. It is a most valuable addition to soups and broths to increase their nutritive qualities. The indications for its use are those of other albumin preparations. Von Noorden particularly advises its use in anemic conditions because he believes they require extra protein nourishment. Riba also has, according to von Noorden, a low purin content, and so is of value in the dietary of gouty patients. Von Noorden states that as much as 110 grams a day of this preparation can be utilized by the body.

Subcutaneous and Intravenous Feeding with Glucose.—KAUSCH (*Deut. med. Woch.*, 1911, xxxvii, 8) advocates the administration of grape sugar solutions by intravenous infusion or by subcutaneous injection in certain conditions that are complicated with persistent vomiting or the loss of great amounts of fluid by the intestinal tract, and that consequently are difficult to feed by ordinary methods. Kausch begins with 1000 cm. of a 2 per cent. solution of glucose for subcutaneous injections, and gradually increases the strength to 5 per cent. He has found that the injection intravenously of 1000 cm. of a 5 per cent. to a 7 per cent. solution is a perfectly harmless procedure. There is no excretion of sugar for several days, and after this period only a small proportion of the glucose is lost by excretion through the kidneys. Kausch found that when the percentage of glucose in the solution was higher than 7 per cent. a glycosuria occurred soon after infusion. However, the amount of sugar excreted was only slight compared to the amount infused. The grape sugar solutions were made in physiological salt solution, and when injected intravenously from

from 4 to 8 drops of a 1 to 1000 adrenalin solution were added. The infusions were much preferred by the patients to the subcutaneous injections. Kausch says that undoubtedly some of the benefits derived were from the saline infusion alone, but that the sugar disappeared and therefore must have oxidized. An amount of extra nutriment up to 500 calories is obtained by this method and this must result in some protection to the body proteins. Kausch relates the history of certain cases of inanition who improved or recovered after these glucose infusions.

Sabromin in Chorea.—MAETZKE (*Deut. med. Woch.*, 1910, xxvi, 1412) reports a single case of chorea favorably influenced by sabromin that had resisted other methods of treatment. The patient received from 3 to 6 tablets daily for a period of three months and also during this time was kept on a strict vegetarian diet.

Experimental and Clinical Observations of the Action of Salvarsan on the Eye.—IGERSHEIMER (*Münch. med. Woch.*, 1910, lvii, 2673) relates his experiments on animals that, according to him, show that salvarsan is non-toxic to the optic nerve. He believes that the toxic action of atoxyl upon the optic nerve is due to phenylarsenate derived from the remedy. He says that salvarsan does not seem to contain phenylarsenate derivatives. He states that cats and dogs are particularly liable to have optic atrophy as a result of the administration of atoxyl, but in his experiments he could find no evidence of any such toxic action upon the optic nerve after the injection of salvarsan. However he did find arsenic in the eyeball after injection of salvarsan. He believes that caution should be used in the administration of the drug for long periods because of this fact, although he does not believe that an arsenical derivative that is toxic for nerve tissue can be split off from salvarsan. He also cites a number of clinical cases in his experience when salvarsan had a curative effect upon syphilitic eye affections.

Antityphoid Inoculation.—RICHARDSON and SPOONER (*Boston Med. and Surg. Journ.*, 1911, clxiv, 8) report 1588 inoculations upon 405 nurses in various training schools for nurses in Massachusetts. As yet there have been no untoward results, and they believe that the inoculated individuals have acquired an increased resistance to typhoid fever that will last for several years at least. They expect in the coming year to extend the influence of these inoculations, especially among nurses and those attendant upon the sick. Furthermore, they have strong faith that the procedure will, within a short time, find increasing favor with the general public, which, exposed as it is to many sources of infection, is in great need of specific protection.

The Effect of Salvarsan upon Cranial Nerves.—EHRlich (*Berlin. klin. Woch.*, 1910, xlvii, 2346) in this article replies to recent communications regarding supposedly toxic effects upon the cranial nerves as a result of salvarsan therapy. He says that of about 30,000 cases that have been treated with salvarsan, there has been only one undoubted case of optic atrophy occurring in a previously healthy eye after the injection. He goes on to say that this occurred in a case of tertiary

syphilis that had previously been treated with arsacetin and enesol, and he believes it to be more than probable that the optic atrophy was produced by these preparations of arsenic. A few cases of temporarily disturbed hearing have been reported, and also evidences of facial involvement have followed the injections. In conclusion, Ehrlich says that these disturbances are not of toxic origin, but are syphilitic manifestations. They are caused by a few isolated spirochetæ remaining after sterilization of the principal mass, and occur likewise after mercurial treatment. The marked clinical symptoms are due to the fact that the cranial nerves are enclosed in bony canals, where they are liable to attacks of syphilitic periostitis. The few spirochetæ remaining are not enough to give rise to a positive Wassermann reaction. Ehrlich emphasizes the importance of the observation that such disturbances disappear after the salvarsan treatment is resumed.

Treatment of Banti's Disease.—BANTI (*Folia Hæmatologica*, 1910, x, 33) bases his article on a careful study of 50 cases of the disease known clinically as Banti's disease, cases that were definitely proved either by autopsy or operation. He divides the disease into three distinct periods. The first period of the disease may last from three to five years, and even as long as twelve years. This period is characterized by the gradual enlargement of the spleen. Less constant, often only slight or occurring late in the disease is the anemia. The anemia is secondary in type, usually with leucopenia with a relative and absolute lymphocytosis. Banti calls especial attention to cases of this type that an operation or autopsy have proved to be free from liver involvement. The second type of cases comprises those with evidence of a beginning congestion of the portal system. This stage of the disease may last for several years. Finally the third stage consists of those cases with symptoms of cirrhosis of the liver associated with a diminution in size of the liver and the appearance of ascites. Banti advances the theory that the disease may be caused by some infectious agent, possibly of bacterial origin, that first causes the characteristic disease of the fibrous tissue of the spleen reticulum, and then there follows the degenerative changes in the follicle and pulp. He attributes the anemia and general weakness to some toxin produced in the spleen, and also to this same cause the subsequent changes in the liver. Banti advocates early extirpation of the spleen as a cure for this disease. He thinks that if this is done in the first stage a large majority of the cases can be cured. If cases are operated upon in the second stage, the beginning cirrhosis of the liver may be arrested. Banti relates the results in 36 cases operated upon. Of 4 patients operated upon in the first stage, 3 were apparently cured after periods of observation during fifteen, six, and five years. Of 22 cases operated upon during the second period, there were 13 cures, some persisting for fourteen, seven, and eight years. There were 4 cures in 10 patients operated upon during the third stage. Banti says that in late operations it is often impossible to remove the spleen and that then splenoplexy and a modified Talma operation is indicated.

PEDIATRICS.

UNDER THE CHARGE OF

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Serum Treatment in Diphtheria.—E. W. GOODALL (*Brit. med. Jour.*, 1911, No. 2615, 292) while regarding antitoxic serum as a specific, believes there are certain limits to its use. While he believes in the importance of early treatment, he has modified his earlier view that the limit of its use is the limit of dosage. After the introduction of this serum, and later the sera for tetanus, the streptococcus, and enteric fever, a symptom complex was found to occur after serum injections in a number of cases. This has been called "serum sickness," and has been found to be due to the serum itself and occurs in about 33 per cent. of the cases treated. The general symptoms are fever and a rash, usually urticarial in nature. Other and more severe symptoms were observed in 3 to 4 per cent. of the cases, namely, acute pain and swelling of the joints, pain in the tendons and fasciæ. These general symptoms rarely set in before one week after the serum injection, and sometimes three weeks. The fever, rash, and occasional arthritic symptoms are known as the "normal reaction," and are due to the horse serum. It is known that the sera of other animals can give rise to the same effects. In the great majority of cases the normal reaction, while unpleasant, is not dangerous. "Abnormal reactions" were next recognized and divided into those following a second injection of serum, and those following a primary injection. Abnormal reactions following a second injection have the usual incubation period of at least one week. This reaction is unusually severe and abrupt. There is faintness and much swelling of the body surface and the mucous membranes from the urticaria. A second type of this class exhibits an incubation period shorter than usual, from twelve hours to six days. This is termed "accelerated reaction" and exhibits severe urticarial swelling, vomiting, prostration, and swelling of the joints. In a third type of this group, called "immediate reaction," the serum reaction appears within a few minutes to five or six hours after the injection, and exhibits an explosive suddenness, high temperature, cyanosis, and rigor. From these facts, therefore, it is deduced that in certain persons injection of a foreign serum leads to increased susceptibility to that serum if repeated. "Abnormal reactions" following a first injection are more severe and often fatal. Gillette collected 30 cases of this kind, 16 of which were fatal. Most of them occurred in the United States. Twenty-two in this series were subject to asthma of some form or other. The symptoms of this class of cases are usually intense dyspnoea, failing respiration, with cyanosis and collapse. They occur shortly after the injection. Goodall believes that an indiscriminate use of the serum as a prophylactic is unjustifiable. A delay of a day or two in doubtful cases not laryngeal is justifiable. In undoubted diphtheria Goodall would hesitate to give the serum only when the patient is asthmatic. If the

disease is severe or the larynx is involved, the choice between the two evils would be to give the serum and risk the possible hypersensitiveness. The earlier the treatment in any case, the smaller the dose necessary. Large doses of calcium lactate tend to mitigate the rash of serum sickness.

Chorea Successfully Treated with Salvarsan.—JOHANN V. BOKAY (*Deutsch. med. Woch.*, 1911, xxvii, 111) reports a case of chorea in a child, aged eight years, which was treated with salvarsan. The chorea was so severe that the child was kept in a padded crib to avoid injuring itself. On November 9, 20 grams of salvarsan was injected subcutaneously and was well taken. On November 11 there was a perceptible diminution in the choreiform movements, and a small, painless, infiltrated area was found at the point of injection. On November 14 a marked improvement in the incoördination was observed and a small, centrally placed area of skin necrosis developed on the infiltrated area. On November 23 the choreiform movements were disappearing rapidly. On November 30 the choreic movements were barely perceptible and the child was up and about. By December 8 the patient was entirely cured and the infiltrated area absorbing. A control case of the same age, but with a less marked chorea, was treated at the same time with Fowler's solution of arsenic, beginning November 9, but by December 12 this case still showed marked choreiform movements, although having had a thorough course of the Fowler's Solution. In the first case, except the infiltration and necrosis at the point of injection, no bad effects were observed from the salvarsan. Bokay does not comment on the quick improvement in his case, but remarks that Rumpel found no improvement in chronic articular rheumatism treated with salvarsan.

Neurasthenia in Children.—CLIVE RIVIERE (*The Practitioner*, 1911, lxxxvi, 38) says that standard examples of neurasthenia are found in older boys and girls, and that slighter forms are common in quite early years, childhood supplying the material out of which adult neurasthenics are made. The preneurasthenic child is usually neurotic, and characterized by overdevelopment of the emotional faculties. An unemotional type marks the other end of the scale, and all grades exist between the two types. The neurotic type presents hypersensitiveness, excitability, emotionability, and timidity. The restrained emotional type is gloomy, solitary, shy, and may be thought dull. The neurotic child is prone to suffer from the functional neuroses, such as night terrors, "tics," and chorea, migraine, epilepsy, asthma, etc., and is peculiarly subject to acute rheumatism. In young children a deficiency of nerve force may be present from earliest childhood, and is characterized by weakness, weariness, poor concentration, and abnormal sensitiveness to climatic conditions. The digestion is weak and capricious, nutrition subnormal, and the hands and feet are habitually cold. The opposite type is the starved neurasthenic, produced by poverty, underfeeding, and loss of sleep, and is characterized by pallor, apathy, and chronic exhaustion. A third type exhibits gastro-intestinal dyspepsia or "mucous disease," combined with neurasthenic symptoms. Treatment of the gastro-intestinal tract does not altogether cure,

where a want of nerve force is primarily responsible. Splanchnic vasomotor paresis, a "pooling" of blood in the splanchnic area, is a marked phenomenon in many cases, and is largely responsible for the feeble circulation, pallor, tendency to faints, and probably intestinal symptoms, including the mucous flux. The treatment of neurasthenia in childhood should be preventive. A non-stimulating, quiet, uneventful childhood is essential. The masticatory instinct must be thoroughly educated to avoid dyspeptic troubles. Schooling is essential, and large public schools are not to be recommended. Underlying causal conditions should be sought and removed; among these are excessive school strain and malnutrition, and overfeeding or "stuffing," especially with sweet carbohydrate "slops." The latter requires a regulated dietary, in a dry form thoroughly masticated, and dietary discipline. Tendency to splanchnic congestion requires special treatment. The feet and legs, if cold, are rubbed and well covered. Daily recumbency for an hour or so is of value. Exercises to strengthen respiratory and abdominal muscles, and a cold sponge or spinal douche are important. Among drugs, occasional use of calomel is valuable. Malt extract and pancreatin are also of value, and digitalis in many cases tends to brace up splanchnic circulation.

Some Points on "Serum Disease."—JOHANN V. BOKAY (*Deutsch. med. Woch.*, 1911, xxxvii, 9), in connection with the injurious effects of serum injections, approves of the term "serum sickness," applied to this condition by v. Pirquet and Shick, who described it as a definite clinical picture. Besides the skin affections are found fever, pain, and swelling in the joints, localized cedema, and albuminuria. Instances of this condition since 1894 indicate that the first signs of this condition appear from eight to ten days after the injection of the serum. However, some cases arise in which these reactions to serum occur much more rapidly, even immediately after the injection. Von Pirquet, Shick, and others have shown that this "accelerated reaction" occurs usually where a condition of "anaphylaxis" exists. There is no doubt that anaphylaxis often causes unpleasant symptoms, and the possibility of serum sickness should always be considered at the bedside when, after an interval, serum injection is again necessary. This is especially true, since all these sera are derived from the horse. Wolff-Eisner has indicated the elimination of anaphylaxis by using serum from another species of animal. Bokay thinks it would be wise if, in the future, diphtheria antitoxin were prepared not only from the horse, but from other animals, as the sheep, cow, and ass. The "accelerated reaction" to serum, Bokay thinks, indicates a previous inoculation of the patient with serum from the same species. He reports 2 cases of diphtheria in children of different families. Neither child had ever had any serum injection. They were both injected with the same quantity of a serum which was prepared at the same time from the same horse. Within a few minutes after the injection, both children broke out in a severe urticarial eruption, covering the face and scattered over the body. This rash faded within a day. These cases cannot be explained on the ground of anaphylaxis. In 1908 about 10 per cent. of cases occurring in Bokay's observation developed serum sickness, and in 1909 there was 23 per cent. In the month of January, 1911, out of 23 cases, 50

per cent. developed a serum exanthem. In all these cases the disease appeared as usual about eight or ten days after the injection. The serum used for these cases came from one lot derived from the same horse. Bokay thinks the cause of the serum sickness in the two children above described was due to some individual element of the horse from which the serum was derived.

OBSTETRICS.

UNDER THE CHARGE OF

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Cesarean Section for Impassable Contraction Ring.—DICKINSON (*Surg. Gyn. and Obstet.*, October, 1910) reports the case of a patient who, in her first labor, had a contraction ring obstruction to delivery which necessitated the use of forceps, followed by the loss of the child. The patient was delivered at the thirty-second week, the obstructing ring did not relax under chloroform, and the death of the child was due to the compression necessitated by delivery. Two years later the patient again came into labor, with pains every half hour for forty-eight hours. The cervix was soft, the membrane detached, the character of the contractions good, the head remaining high, with the occiput posteriorly and the back to the left. A contraction ring of the thickness of the thumb, admitting two fingers, lay just above the pelvic brim two inches beyond the softened cervix, and surrounding the entire circumference of the uterus. No internal os, apart from this upper circle, could be located. The lower segment was relaxed but was not thinned. Morphine, and attempts at dilatation under surgical anesthesia, failed, and uterine contraction was constant, but with each active pain the contraction ring hardened perceptibly. The membranes had ruptured a few hours previously, and the general condition of the mother and child was good. As the parents were desirous of obtaining a living child, section was chosen and was successful. The ring retained its contraction after the emptying of the uterus.

Dickinson also reports an operation in a primipara for a similar condition, which was successful. Two cases operated upon by Watt are also reported. In the first of these, two attempts had been made to deliver with forceps, but the writer believed, as aseptic precautions had been employed, that these attempts had not seriously jeopardized the results of the Cesarean operation. Section was accordingly performed. The mother died of septic peritonitis on the ninth day, but the child survived. The second case was a primipara of more than usual muscular development, upon whom delivery with forceps was tried with negative results. On admission to hospital the occiput was found posteriorly, and the forceps was again tried; this attempt was repeated but without success. Section was performed, the mother dying twelve hours after operation, but the child survived.

Dickinson collected 6 cases of section, reported in the literature of the subject, done for contraction ring; 3 of the 6 mothers died; two children survived—the two that were living when the operation was undertaken. One of the mothers who died was an eclamptic; in the case of the other two, the operation had been delayed and the patients had been subjected to previous efforts at delivery. In some of the more desperate cases reported, hysterectomy was successful. Dickinson believes that the contraction ring is the lower edge of the muscle of the body of the parturient uterus in action. It makes no clinical difference whether the ring is an anatomical internal os or not. Its presence is a physiological occurrence, resulting from normal activity, which is in excess, or from unbalanced development, and in either case it may constitute a slight or serious obstacle to delivery. In its least degree it is physiological and gradually disappears as the foetus passes out of the uterus. In a greater degree, it is an hour-glass narrowing in the later stages of labor, its tension and resistance increasing during each pain. The body of the uterus shortens and thickens throughout its entire wall. In its most pronounced development, it is a part of tetanus of the uterus developing late in labor. The ring either retains the foetus in the uterine body, leaving the lower uterine segment empty, or encircles part of the foetus, usually the neck, the head moving in the lower segment. When fully developed, it may be palpated externally as it rises in the abdomen, or may be determined by vaginal examination. One-third of the mothers and one-half of the children died in the reported cases. The most important factor affecting mortality is early recognition of the complication. As the obstruction is more distant from the exit than any other whatever, it demands an operation, which can safely be performed from above. If the child be dead, the spasm can usually be relaxed by morphine and complete ether narcosis, and the child removed by vaginal procedure. In some cases even embryotomy and basiotripsy have failed to empty the uterus, and in fear of septic infection, hysterectomy was performed. In a case not infected with a dead foetus retained behind an undilatable ring admitting but two fingers from above the pelvic inlet, Cesarean section should be performed, and not embryotomy, if the patient can have hospital care. If the child be living, a persistent effort should be made to dilate the ring by rest, morphine, surgical anesthesia under ether, and patient manual dilatation. In head cases, a fair essay of forceps, short of the risk of cerebral hemorrhage, and combined with expression, is undertaken. In transverse cases, version should be attempted, bearing in mind the risk of rupture. If the forceps fail in head cases, and version cannot be performed in transverse, the foetal heart being good and the cord unharmed, choice is made between embryotomy and section. Embryotomy will usually be chosen because of the frequency of lowered vitality in the child, when accessibility favors this operation, and because of the lessened risk to the mothers in most instances. With mother and child in fair condition, with infection unlikely, with a ring not yielding to a combination of morphine, etherization, and manual dilatation and contraction, Cesarean section is indicated in preference to embryotomy, and should be undertaken if the parents elect a somewhat increased risk for the sake of the child. Cesarean section is safer

than embryotomy in the worst degrees of ring contracture and tetany located high, provided infection is improbable.

[The reviewer would call attention to these cases as illustrating a fact which he believes is being constantly demonstrated in obstetric practice. It will be observed that in this report of cases those in which forceps or version had been tried necessitated hysterectomy, or without this, died from infection. Increasing experience confirms the reviewer in the belief that the application of forceps or attempts at version makes the performance of the conservative Cesarean section unjustifiable. No matter how careful the operator may be in his personal asepsis, such manipulation carries into the uterus bacteria from the vagina, which become pathogenic, and traumatism is inevitable in these manipulations. The decision to perform Cesarean section should be made before resorting to forceps, version, or manual dilatation. In these cases there is no necessity for manual dilatation if section is to be performed, as there is sufficient dilatation to permit the drainage of the lochial discharge. If attempts at version or forceps or manual dilatation have been made and have failed, and Cesarean section is to be performed, hysterectomy is indicated. Such cases are preëminently hospital cases, and are more dangerous than pelvic contraction, because the obstacle to delivery is not apparent.—E. P. D.]

Cesarean Section under Local Anesthesia.—SMITH and SCHWARZ (*Surg., Gyn., and Obstet.*, October, 1910) report 2 cases of Cesarean section under local anesthesia. The first was that of a primipara having a kyphotic and scoliotic spine, mitral regurgitation, chronic nephritis, and a funnel-shaped, generally contracted pelvis. The second case had a generally contracted pelvis, showing some traces of rachitis. The patients agreed to local anesthesia, with the understanding that should pain be felt, gas and oxygen were to be administered. The solution used was $\frac{1}{2}$ per cent. of novocain in normal salt solution, to each 10 c.c. of which was added one drop of 1 to 1000 adrenalin solution. This was freshly made and boiled for five minutes, just before using. Two points, one 9 cm. above the umbilicus, and the other a like distance below it in the median line, were infiltrated with a drop of the solution, and from these, as points of departure, the solution was injected about a diamond-shaped area subcutaneously, and then subfascially. The line of the incision was not infiltrated in either of these cases. The amount of the solution used was about 75 c.c. in one case, and 60 c.c. in the other. The operation was performed by opening the uterus *in situ* and removing the child and placenta. The uterus was then lifted out of the abdominal cavity and surrounded by pads dipped in hot saline solution. In the first case the cervix was dilated by the finger passed through the uterine incision, followed by Goodell's dilator. In both cases there seemed to be absolute absence of pain throughout the operation, notwithstanding the dilatation of the cervix from within the uterus in the first case, and the squeezing of the uterus forcibly in the second case, to see if pain could be produced. There was slight loss of blood, although no ligature was passed about the uterus, nor were the broad ligaments compressed. It is not believed that the local anesthesia had anything to do with this. Neither patient suffered shock, and each had practically a normal convalescence.

GYNECOLOGY.

 UNDER THE CHARGE OF

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A New Method of Replacing the Retroflexed Uterus.—GOLDBERG (*Zeit. f. Gyn.*, 1910, xxxiv, 1645) describes the following method which has been useful in his hands. A sharply bent Hodge pessary of the proper size is introduced into the vagina so that the broad end lies firmly against the posterior vaginal fornix. With the palmer surface directed upward, the index and middle fingers of the left hand are introduced between the pessary and the anterior vaginal wall as far as the cervix where the fingers are separated the width of the portio. By means of the dorsal surface of the fingers, pressure is made backward on the anterior small end of the pessary. Gentle abdominal manipulation with the right hand will easily bring the uterus forward. Especially adaptable for this method are those cases of retroflexion associated with relaxation of the uterine ligaments and surrounding tissues. In nullipara with hypoplastic retroverted uteri is reposition impossible by any method; a short portio and flat vaginal fornix render this method unsuitable.

Arteriosclerosis of the Uterine Vessels.—CHALFONT (*Jour. Amer. Med. Assoc.*, 1911, lvi, 239) has made a study of eleven uteri removed on account of repeated hemorrhages unassociated with neoplasm and three uteri from multiparæ presenting a normal menstrual history. He concludes that proper uterine contraction is essential to the control of uterine bleeding. There is no definite pathological condition present in these cases that is not found in others not giving any history of hemorrhage, with the possible exception of the increase in number and size of vessels. Some loss of functional power of the uterine muscle is the predisposing cause of bleeding in cases of arteriosclerosis. This loss of functional power is due either to the development of fibrous and elastic tissue from subinvolution or to the condition which caused this subinvolution. The exciting causes are probably many. Chalfont suggests the increase in size and number of vessels, general increase in blood pressure from kidney disease or general arteriosclerosis, passive congestion from heart disease, local congestions or general muscular weakness.

The Utilization of the Anterior Cervical Wall in the Operation for Vesicovaginal Fistula.—KUSTNER (*Zeit. f. Geb. u. Gyn.*, 1910, lxxvii, 603) devotes fifty-two pages to the description of his operative technique for the cure of vesicovaginal fistula and to the analysis of 50 cases which he has operated upon by this method. Briefly summarized, the operation consists in freeing the bladder from the cervix, denuding the vagina around the fistula, and uniting the vaginal cuff to the cervix by interrupted, non-absorbable sutures. This procedure is applicable to any form of vesical fistula, does not sacrifice tissue,

utilizes the anterior cervical wall as a splint, and avoids all risk of injury to the ureters. Of the 50 fistulæ reported, 5 were cervicovesical, 14 cervicovesicovaginal (cervical defects), and 30 vesicovaginal. Primary healing resulted in 46 cases, while 4 required a second operation.

An Experimental Study of Ascending Genital Tuberculosis.—In order to substantiate his previous assertion that genital tuberculosis may be due to an ascending infection, JUNG (*Archiv f. Gyn.*, 1910, xcii. 764) reports the results of his experiments in 33 rabbits. The inoculations of tuberculous material were made either into one uterine horn or into the vagina, under such precautions as would prohibit direct injection into the uterine cavity. In the selection of his specimens for microscopic study, he excluded those which showed peritoneal tubercles, since the objection could be made that the infection had extended from without inward and not by way of the uterine cavity. The author has been able to demonstrate five instances of true ascending tuberculous infection. Careful study of the preparations afforded no evidence of congestion of the uterine secretion which might act as a provocative factor, an assertion which Baumgarten denies. In a supplementary article (page 775) Engelhorn offers further proof of the possibility of an ascending infection. Following the injection of earmine into the vagina, the rabbits were killed at varying intervals and the pigment could be plainly seen in the mucosa, muscularis, or subperitoneal tissue, depending upon the length of time elapsing after the injection. In the human, hematogenous infection is the rule; in rare cases a primary ascending genital tuberculosis undoubtedly exists.

Active Substances in the Uterus and Ovary.—SCHICKELE (*Münch. med. Woch.*, 1911, lviii, 123) has carried out a series of experiments with extracts of the uterus and ovaries in order to determine their action upon the coagulability of the blood. These extracts were obtained by subjecting the organs to high pressure—four to five hundred atmospheres. He has been able to demonstrate conclusively that coagulation is decidedly retarded; this was especially marked with extracts of uteri which had been extirpated on account of profuse hemorrhage from myomata or metrorrhagia associated with no demonstrable lesion when coagulation did not occur in from six to twenty-four hours. While extracts similarly obtained from other glands of internal secretion produced a delay in the coagulation time, this was in no way comparable to the action of the uterine and ovarian substances; extracts from the corpus luteum were especially active, as evidenced by the fact that coagulation did not take place in twelve days. The author also tested the effects of these extracts given intravenously, and found that an intense lowering of blood pressure followed as the result of peripheral dilatation of the bloodvessels, often associated with delay in the coagulation time. Twitchings and even convulsions were often accompanied by partial unconsciousness; with a more intense action, the respirations and pulse became slower, and in some instances death of the animal rapidly ensued.

Some Observations on the Operation of Abdominal Myomectomy for Myomata of the Uterus.—W. J. MAYO (*Surg., Gyn., and Obstet.*,

1911, xii, 97) bases his remarks upon an experience of 1244 operations for uterine myomata. In patients between the ages of twenty and thirty years myomectomy is the operation of choice unless the ovaries are sufficiently diseased to require removal when hysterectomy is indicated; between thirty and forty years, each case must be judged upon its own merits, and the wishes of the patient should be an important factor in deciding upon the type of operation; between forty and fifty years hysteromyomectomy is the wiser procedure. The most serious objection which has been offered against myomectomy is the increased mortality from sepsis and hemorrhage. Care in avoiding undue suture tension will lessen the chances of infection; hemorrhage is best controlled by a continuous catgut suture. Should oozing from the needle puncture follow myomectomy in a pregnant uterus, the tip of the omentum may be used as a pressure pad along the line of suture. Curettement of the uterus through an incision in the anterior wall has been found very useful; in several cases the removal of a polypus which had caused severe hemorrhage, avoided hysterectomy. No fatalities and but one miscarriage followed myomectomy during pregnancy. Only seldom must the uterus be emptied when myomata complicate pregnancy, and hysteromyomectomy with the non-viable child is one of the rarest necessities, because myomectomy usually suffices. At term, in cases where myomata obstruct the pelvic outlet, the Porro operation is indicated. A table of the various operations and results is appended.

Carcinoma of the Uterus.—SCHAUTA (*Med. Klin.*, 1911, vii, 6) mentions the various methods which have been devised for the treatment of carcinoma of the uterus, such as drugs, ferments, cauterization, fulguration, etc., and states that these remedies have at best only a palliative action. The knife offers the only hope of cure. In order to obtain uniform statistics, he has practically limited himself to the vaginal route, and his results compare favorably with the radical abdominal operation of Wertheim. The primary mortality has been reduced from 10 to 4 per cent.; the operability is between 50 and 60 per cent.; 40 to 50 per cent. have been permanently cured, and in his last series of cases the absolute cures will be 28 per cent., four years elapsing since operation. These figures show that even in the most skilled hands only 20 to 25 out of every 100 cancer patients can be cured. How can these results be improved? The acme of technical skill and radical excision has been reached; the only avenue of improvement lies in early diagnosis of the disease and immediate operation. The brunt of responsibility must fall upon the general practitioner, to whom the patient usually presents herself first; an examination should be made of all patients who present irregularities during the menopause, in order to rule out cancer. Further, education of the public is necessary; the objection that undue fear will be aroused in the mind of the public is more than offset by the number of lives that will be saved.

Epidural Injections in Sacral Pains.—ALBRECHT (*Zent. f. Gyn.*, 1911, xxxv, 50) has employed epidural injections of normal salt solution in 53 cases of sacral pain unassociated with gross disease of the genitalia. In 38 cases the pain was completely relieved by one injection, while in

15 cases little or no benefit resulted. In most instances various forms of treatment had been used with no benefit. Out of 16 cases of purely functional neurosis, one injection was curative in 9; no improvement followed in 2 cases. Success followed one injection in 3 cases of retroflexion which operation had failed to influence. The sacral pain was completely relieved in 11 out of 13 cases of chronic inflammatory disease of the adnexa and parametria. Two out of 3 cases of enuresis were cured by one injection. From his observations he concludes that epidural injections of normal salt solution are indicated in those cases of sacral pain where the absence of a demonstrable pelvic lesion makes local or operative treatment useless and where the other usual methods have failed. Further, he recommends the injection for the treatment of functional bladder conditions as well as essential pruritis vulvæ and coccygodynia.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Relative Importance of the Bovine and Human Types of Tubercle Bacilli in the Different Forms of Human Tuberculosis.—PARK and KRUMWIEDE (*Jour. Med. Research*, 1910, xxiii, 205) report the results of an extensive statistical study of 43 strains of tubercle bacilli obtained from unselected cases of tuberculosis in human beings. Most of the material was derived from the New York hospitals. They conclude that tubercle bacilli isolated from man fall into two groups; one of these groups is identical in all its characters with that found in cattle, and consequently they differentiate two groups which have been designated human and bovine types. Each type shows certain differences, the most important for separation being found culturally and in virulence. The great majority of cultures group themselves around two extremes, though there are a few cultures showing variant characteristics. There is no overlapping of the characteristics; these two types are probably different because of residence in different hosts over long periods of time, and as such are stable. Though observations have been recorded to show that a rapid change of type may take place, these experiments are incomplete and inconclusive, and no confirmation of such results could be obtained by the authors. The result of this study showed that of the 436 cultures examined, 403, or something over 90 per cent., were of the human type. Only one culture of bovine type was found in an adult, and that in a case of genito-urinary tuberculosis; 9 cultures of the bovine type out of a total of 54 occurred in children from five to sixteen years of age, and 22 cultures out of a total of 84 occurred in children under five years of age. It may thus be seen that the bovine type of tubercle bacillus occurs most frequently early in life, over 26 per cent. of the cases of tuberculosis in children under five years of age showing

this type of bacillus. The bovine type of bacillus was found most frequently in cervical tuberculous adenitis, though it was also found in abdominal tuberculosis, in generalized tuberculosis of alimentary origin, in generalized tuberculosis, and tuberculous meningitis. These valuable statistics, the largest that have been accumulated by any one writer, added to the collected statistics, give a total of 1042 cases of tuberculosis in which the type of organism has been identified.

The Presence of a Diastatic Ferment in Leukocytes.—It was first shown by Bial in 1892 that the blood and lymph contained a ferment which was capable of digesting starch. Later, this was fully confirmed by others, but there has been much discussion concerning the origin of this enzyme. The theory that it came from the pancreas or from the liver, which was also shown to possess diastatic properties, seemed most probable. HABERLANDT (*Pflüger's Arch.*, 1911, cxxxii, 175) has recently published some investigations which throw very definite light upon, at least, one possible source of the diastatic ferment of the blood. Working at first with cold-blooded animals, he was able to show that the lymph from the lymph sacs of frogs was capable of digesting starch. Different starches, however, showed various grades of susceptibility to this ferment. Amylen, a starch from wheat was most easily affected, whereas the starches from potato and rice were much less readily acted upon. Microscopically the lymph contained a few leukocytes and by studying these cells it was possible to make out that they ingested the starch granules. Later the starch granules underwent dissolution within the protoplasm of the cell. By increasing the number of leukocytes in the lymph the amount of digested material increased. There was, however, always some digestion of the starch granules, even though the lymph was free of cells. The ferment action was therefore not wholly dependent upon the presence of leukocytes. The same ferment was demonstrated in the subcutaneous tissues and tissue juices of rabbits, and here again the action was increased by the presence of leukocytes. It was thought possible that the ferment which was present in the serum, and tissue juices might rise from destruction of cells, and therefore the relative amount of enzyme was estimated in blood plasma in fresh serum and in blood serum which had stood for twenty-four hours in contact with the clot. The proportion of ferment, however, was equal in each instance, and therefore it did not seem probable that the enzymes were liberated to any amount from the leukocytes during the production of the blood clot.

The Action of Diuretics upon Diseased Kidneys.—In a previous article (*Deut. Arch. f. klin. Med.*, 1909, xcvi) HEDINGER and TAKAYASU have shown by means of experimentally induced nephritis that the kidney reacts differently toward certain diuretics, according to the toxic agent which is used to induce the nephritis. Chrome salts, sublimate, and uranium nitrate are toxic agents which attack first the tubular epithelium and leave at first the vessels undamaged. In the early stages of this tubular form of nephritis salt solution and caffeine, when ingested, cause an increase in the volume of the kidney with diuresis. Cantharadin and arsenic, on the other hand, attack primarily the bloodvessels of the kidney and set up a vascular form of nephritis.

In the early stage of this vascular nephritis, neither salt solution nor caffeine produces any increase in the volume of the kidney or diuresis. The ability of a substance to produce diuresis seems, therefore, dependent upon the ability of the bloodvessels of the kidney to react to stimuli. Hedinger (*Deut. Arch. f. klin. Med.*, 1910, e, 305) has now extended these experiments and has studied the diuretic action of other drugs in experimental nephritis, and especially the digitalis derivatives. Recently Jones and Loewi have shown that small doses of digitalis have a diuretic effect in normal animals. This does not take place, as was once supposed, through increased heart action, but by a dilatation of the kidney vessels through a direct action of the drug upon the vessels. Hedinger used for his experiments digipuratum, digalen, theophyllen, and sodium chloride. The injections were made intravenously. In the normal rabbit, digipuratum and digalen produced very slight increase in the volume of the kidney and scarcely any appreciable diuresis. Theophyllen caused decided increase in kidney volume with diuresis, while the same effect, though a much more marked one, occurred with sodium chloride. In the early stages of the tubular form of nephritis, caused by chrome salts, both the digitalis derivatives produced increase in kidney volume and much more diuresis than was observed in normal rabbits. Theophyllen and sodium chloride acted in the same way. In animals suffering from uranium nephritis the same increase in kidney volume and diuresis was observed in the early stages, but very soon, as the kidney lesion progressed, this disappeared. In the true vascular type of nephritis caused by cantharadin, none of these drugs showed the slightest ability to increase the kidney volume or to cause diuresis. In no instance did any of the drugs cause any change in blood pressure. In the first stages of the tubular form of nephritis the bloodvessels of the kidney respond more readily, therefore, to small doses of digipuratum and digalen than the bloodvessels of the normal kidney, and consequently an active diuresis is set up. Later in the intoxication and when the vessels are severely injured, as in cantharadin nephritis, even the most active diuretics become ineffective.

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MAY, 1911.

ORIGINAL ARTICLES.

THE ANATOMICAL EXPLANATION OF THE PARALYSIS OF THE
LEFT RECURRENT LARYNGEAL NERVE FOUND IN
CERTAIN CASES OF MITRAL STENOSIS.¹

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DURING the past thirteen years there have been reported 37 cases of mitral stenosis with associated interference with or abolition of the movements of the left vocal cord. Study of the notes of those cases which came to autopsy shows so much variation in the structures which are described as causing pressure on the left recurrent laryngeal nerve that the present study was undertaken with the idea of attempting to clear up the discrepancies. Our work has consisted of an analysis of all the cases reported up to the present time, and of a careful examination of sections and dissections of hardened thoraces. Observations made in soft bodies are of questionable value, because the opening of the chest allows of so much collapse

¹ Read at a meeting of the College of Physicians of Philadelphia, March 1, 1911.
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and the manipulations of dissection cause such a degree of distortion that normal relations are altered to a most astonishing degree. We therefore used only cadavers with everything hardened *in situ* by means of an arterial injection of formaldehyde solution, in the endeavor to keep the thoracic and especially the mediastinal viscera as nearly as possible as they are *in vivo*.

HISTORICAL. The association of paralysis of the left recurrent laryngeal nerve with mitral stenosis was first described by Ortner, in 1897, as occurring in two cases which had come under his observation. He ascribed the paralysis to compression of the nerve between the arch of the aorta and the distended left auricle. The nerve in his cases was discolored, compressed, and ribbonlike. In the following year Herriek recorded a case in which, in addition to a dilated left auricle, chronic adhesive pericarditis was found, the nerve being embedded in a mass of cicatricial tissue as well as compressed by the auricle.

In 1901 Kraus reported a case of left recurrent paralysis associated with mitral stenosis. He took exception to the anatomy of Ortner's explanation, and described the mechanism in his case quite differently, taking the ground that the laryngeal paralysis, although associated with marked left auricular dilatation, was indirectly due to hypertrophy of the right ventricle. This condition, by altering the position of the heart as it lay on the diaphragm, was assumed to alter the relationship between the pulmonary artery, the aortic arch, and the aortic ligament in such a way as to cause the ligament to drag upon the recurrent laryngeal nerve. In his case the aortic ligament is stated to have run more horizontally than is normal, so that the left recurrent laryngeal nerve did not course laterally from the aortic ligament around the aortic arch, but crossed the latter.

At the point at which the nerve crossed the aortic ligament it was constricted and discolored.

In v. Schroetter's case the nerve is reported as having been compressed between a patulous ductus arteriosus and the aortic arch, and in Frischauer's case, between the left pulmonary artery and the aorta, the former being pushed upward by the dilated left auricle. Hofbauer described the compression as occurring between the dilated pulmonary artery and the aorta, while in Bonardi's and in two of Osler's cases we are again told that the left auricle impinged directly upon the aorta. In Osler's third case there was no autopsy.

In Gantz's case the nerve is stated to have been pressed upon by enlarged peribronchial and peritracheal glands. Despite the co-existence of a severe pneumonia and pleuritis, he attributes this glandular enlargement to stasis produced by a weak heart. No similar explanation is to be found in the literature of the subject. In Mead's case the compression was presumably exerted by the

greatly dilated pulmonary artery, although a patulous ductus arteriosus was also found.

Little of clinical interest is reported concerning the laryngeal symptoms, although in some of the cases it was noted that the hoarseness was more marked in certain positions. Thus, Hofbauer's patient was less hoarse in the dorsal and right lateral postures, while Protas's² was more hoarse when the head was rotated to the left.

The paralysis may apparently be bilateral. In seven of Quadrone's eight cases both cords were paretic. In explanation of this he assumes that the brachiocephalic and subclavian arteries may sustain the brunt of the cardiac displacement. It is on this basis that the inequality of the radial pulses sometimes met with in cases of mitral disease has been explained (pressure of the auricle upon the aortic origin of the left subclavian artery). Thus, Masser³ and Perotta hold that right-sided recurrent paralysis in mitral stenosis is never found as an isolated or primary lesion, but only as an exaggeration of those conditions which brought about the left recurrent paralysis. As a matter of fact, the entire situation, especially when the right recurrent is concerned, is so clouded that it is eminently desirable that future autopsies should be made with greater care, or, as Kraus has suggested, not made as routine autopsies, but as frozen sections. None of the cases in which the right nerve was implicated have come to autopsy.

ANATOMIC CONSIDERATIONS. The left recurrent nerve springs from the vagus as the latter is passing down the sinistro-anterior aspect of the horizontal part of the aortic arch (Fig. 1). It hugs the aorta closely and passes under the arch either at the point at which the ligamentum arteriosum joins the latter vessel or slightly anterior to this position (Fig. 1). Reaching the dextro-posterior side of the arch, it ascends, its further course having no bearing on the clinical condition under discussion.

The bifurcation of the pulmonary aorta takes place at the lower inner margin of the left bronchus, about 2.5 cm. from the bifurcation of the trachea. The angle lies behind the left margin of the ascending part of the aortic arch and above and in front of the root of the left upper pulmonary vein (Figs. 2 and 3). The right branch passes horizontally to the right under the aortic arch and above the left auricle. It does not enter the present problem. The left branch curves over the left superior pulmonary vein and the left bronchus, both of which it indents, and passes outward and markedly backward, forming an angle with the right branch of about 100 degrees in the horizontal plane. Above, and 4 mm. away from it is the beginning of the descending part of the aortic arch, to which

² "Su due casi di emiplegia laryngea con singulare disturbo disfonico." Atti del Terzo Congresso d. Soc. Italiana di Laringologia, 1899, p. 230. (No pathological findings in thorax in either case clinically. No autopsies.)

³ Quoted, Boinet, l. c.

it is connected by the ligamentum arteriosum (Fig. 1). The descending part of the arch continues down in contact with the posterior mesial surface of the left pulmonary artery. Below the left pul-

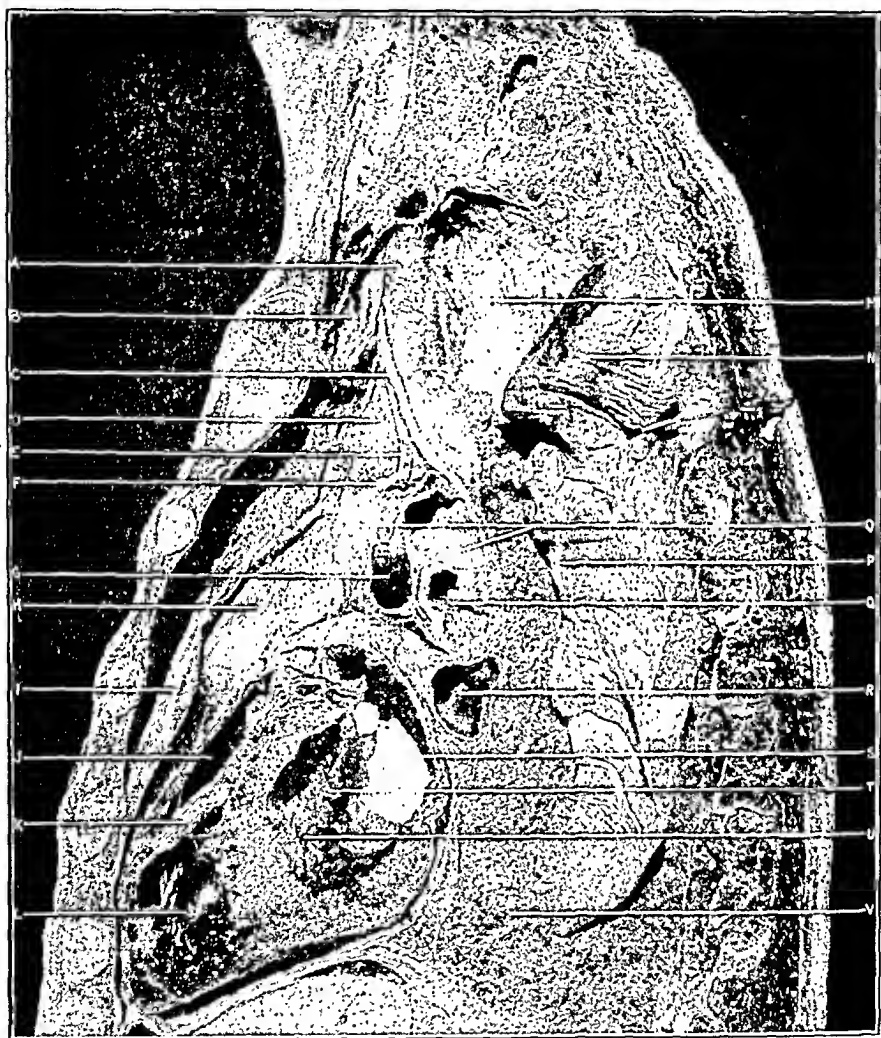


FIG. 1.—Sagittal section 3 cm. to the left of the midsternal line, viewed from the left: *A*, left subclavian artery; *B*, retracted pleura; *C*, left vagus nerve; *D*, arch of aorta; *E*, left recurrent laryngeal nerve; *F*, ligamentum arteriosum; *G*, left superior pulmonary vein; *H*, pulmonary aorta; *I*, reflected pericardium; *J*, right ventricle; *K*, moderator band; *L*, right ventricle; *M*, apical mediastinal pleura; *N, P*, retracted upper lobe of left lung; *O*, left pulmonary artery; *Q*, left bronchus; *R*, left inferior pulmonary vein; *S*, left auricle; *T*, mitral leaflet; *U*, left ventricle; *V*, cut surface of left lower lobe.

monary artery lie the left superior pulmonary vein and the left bronchus (Figs. 2 and 3).

The appendix of the left auricle is curled around the root of the pulmonary aorta. It projects upward in the angle between the left pulmonary artery and the left superior pulmonary vein (Fig. 4).

The ligamentum arteriosum (the obliterated ductus arteriosus) is a fibrous cord, about 3 mm. thick and 2 cm. long. We have found that it lies almost exactly in the antero-posterior plane of the body and ascends but slightly as it passes backward from the left pulmo-



FIG. 2.—View of a dissection of the posterior mediastinum from behind: *A*, left subclavian artery; *B*, left recurrent laryngeal nerve; *C*, aorta; *D*, left pulmonary artery; *E*, left superior pulmonary vein; *F*, left inferior pulmonary vein; *G*, left ventricle; *H*, aorta (reflected); *I*, left bronchus (reflected); *J*, right bronchus (reflected); *K*, cut end of esophagus; *L*, superior vena cava; *M*, descending part of aortic arch; *N*, ligamentum arteriosum; *O*, angle of bifurcation of pulmonary aorta; *P*, right pulmonary artery; *Q*, left auricle; *R*, right superior pulmonary vein; *S*, right middle pulmonary vein; *T*, right inferior pulmonary vein; *U*, inferior vena cava; *V*, esophagus (reflected).

nary artery to the aorta (Fig. 1). In or slightly anterior to the obtuse angle formed at its junction with the latter vessel lies the recurrent laryngeal nerve.

In effecting pressure on the nerve there are two conditions at work

—increase in size and alteration of position, both dependent upon the narrowing of the mitral orifice. Changes in size, viz., enlargement, involve in sequence the left auricle and appendix, the pulmonary veins, and the pulmonary arteries. The obstruction to the blood current in the mitral orifice results, first, in a dilatation of the



FIG. 3.—Oblique view from the right of a dissection of the mediastinal viscera from behind: A, aorta; B, left pulmonary artery; C, left superior pulmonary vein; D, left inferior pulmonary vein; E, left ventricle; F, thoracic aorta (reflected); G, left recurrent laryngeal nerve; H, superior vena cava; I, angle of bifurcation of pulmonary aorta; J, root of right superior pulmonary vein; K, M, left auricle; L, right inferior pulmonary vein; N, coronary sinus; O, esophagus (reflected).

left auricle and its auricular appendix. Rise of pressure in this chamber is followed by the same condition in the pulmonary veins, which results in their overfilling and distention. This in time dams back the blood in the lungs and tends to cause its stagnation in the pulmonary artery and in the right heart. In consequence there is always present a dilatation of the left auricle and of the pulmonary

arteries and veins, which gives rise to a crowding of the mediastinal structures at the base of the heart.

Changes in position are mainly due to the distention of the auricle, although this can be aided materially by enlargement of the right heart, particularly of the ventricle. Some remarkable instances of left auricular dilatation have been recorded. According to Witwicki,⁴ the left auricle is the most distensible of all the heart chambers, and Samuelson⁵ has stated that occlusion of the left coronary artery causes a flaccid dilatation of the auricular walls, which may

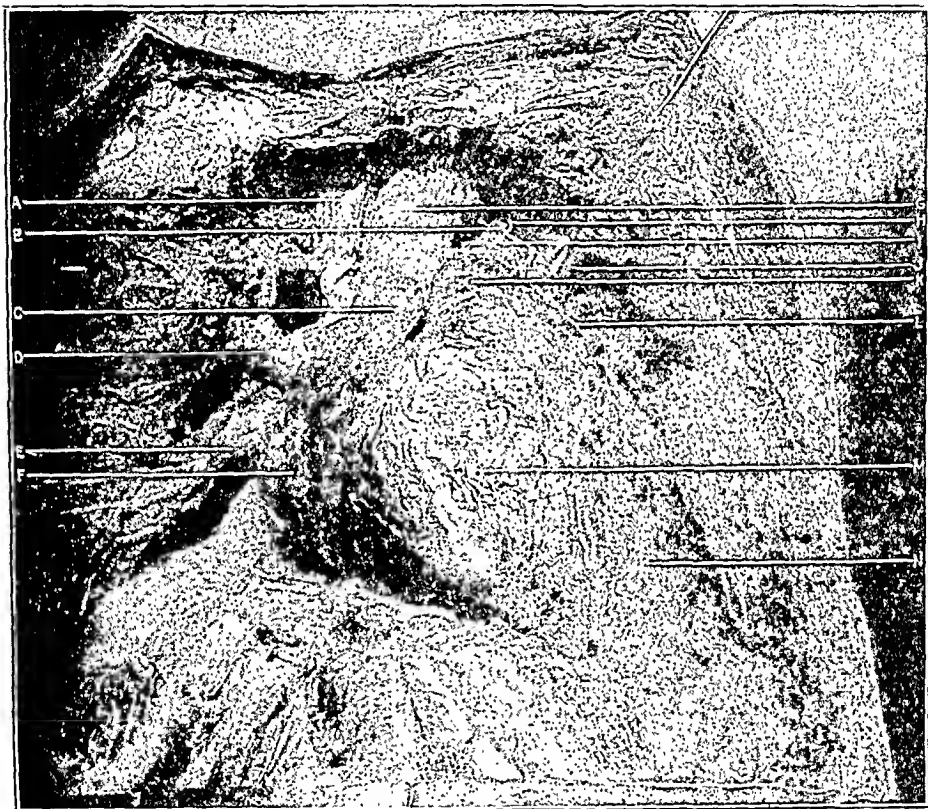


FIG. 4.—View of a dissection of the mediastinal viscera from in front: *A*, anterior vena cava; *B*, ligamentum arteriosum; *C*, right auricular appendix; *D*, right superior pulmonary vein; *E*, right inferior pulmonary vein; *F*, right auricle; *G*, arch of aorta; *H*, left recurrent laryngeal nerve; *I*, left pulmonary artery; *J*, left superior pulmonary vein; *K*, pulmonary aorta; *L*, left auricular appendix; *M*, right ventricle; *N*, left ventricle.

assume the appearance of a distended bladder. Minkowski⁶ removed a heart at autopsy which contained about 4 liters of blood, of which nearly 3 were found in the left auricle. This specimen was obtained from the body of a man, aged thirty-two years, who had suffered from double mitral and tricuspid lesions and in whom a diagnosis of mitral stenosis had been made fourteen years before his death.

⁴ Zeit. f. klin. Med., 1895, xxvii, 321.

⁵ Soc. Anat., Paris, vol. ii.

⁶ Münch. med. Woch., 1904, p. 182.

Despite this enormous dilatation the patient had been able to walk about until but shortly before his demise. The auricular walls were thin and membranous. In the case reported by Briquet⁷ the left auricular capacity was 650 c.c. (the normal average being 55 c.c.), or what is practically equal to the capacity of a whole normal heart. Müller⁸ has recorded an instance in which the left auricle was larger than a child's head, this occurring in a case in which the heart weighed 620 grams, the patient weighing only 65 kilograms. (Under normal circumstances a patient of this weight should have a heart weighing about 300 grams). Toledano⁹ reported a case in which the auricle measured 12 by 11 cm. Sansom has described the auricular wall as being attenuated to the thinness of a visiting card. Owen and Fenton¹⁰ have reported a left auricle with a capacity of 900 c.c., a distention so great that aspiration was performed in the belief that a pericardial effusion was present.

It is well known that dilatation of the pulmonary artery is often encountered in long-standing cases of mitral stenosis, and not infrequently the artery undergoes considerable arteriosclerotic change. In these cases there is an area of dulness at the upper left margin of the sternum, sometimes sensitive to pressure or percussion, as well as enlargement of the right heart. Dmitrenko, in his case of pressure paralysis, succeeded in making graphic records of the pulmonary pulsation.

The left auricular cavity can expand readily in but one direction, viz., upward (Figs. 2 and 3); posteriorly, it rests against the aorta and esophagus; anteriorly, it is limited by the right auricle and the left ventricle, and below by the right auricle and the liver. In expansion, the auricular appendix would probably be the first part affected, as it lies free and unadherent to anything. Should it become dilated it would press upward and backward, thrusting the left pulmonary artery against the aorta, the left upper pulmonary vein against the left pulmonary artery, and forcing the distal portion of the latter against the aorta. Later, when the atrium or main cavity of the auricle dilates, the proximal part of the left pulmonary artery is jammed upward and backward, mainly by the root of the left upper pulmonary vein. The nerve is thus squeezed between the artery on the one hand and the aortic arch or the ligamentum arteriosum on the other. Frischauer and Hoffbauer are the only ones who report finding this post mortem.

COMMENT ON PREVIOUS EXPLANATIONS. The foregoing facts should make us extremely cautious in accepting the reports of non-autopsied cases as examples of recurrent paralysis due to auricular pressure in the course of mitral stenosis. It should be borne in mind that the first examples of this condition were first reported

⁷ "De l'état du cœur gauche dans les lésions mitrales," Thèse de Paris, 1890.

⁸ Zeit. f. klin. Med., 1905, lvi, 520

⁹ Soc. Anat., Paris, 1875.

¹⁰ Clinical Society, London, May 24, 1901.

fully thirty-five years after paralysis of the recurrent laryngeal nerve had first been described by Tuerck and Gerhardt (1862). Furthermore, the details of the cases reported by Koellreuter, in which the paralysis was in all probability due to a mediastinal neoplasm, and by Gantz and ourselves, in which glandular enlargement was the etiologic factor, clearly show how closely the picture produced by mitral stenosis may be simulated by other causes and conditions.

The junior author has for the last six years been especially on the lookout for this conjunction of pathological conditions, and among many hundreds of cardiac patients seen during this time has met with only one case in which recurrent paralysis appeared to be due to mitral disease. There was, however, no autopsy, and the few notes which were made have been lost.

How easily one might be led into attributing left recurrent laryngeal paralysis to mitral stenosis is also illustrated in the following case, which occurred in the service of Dr. F. H. Klaer, in which a diagnosis of mitral stenosis was readily made and in which aortic aneurysm was suspected but later abandoned as the result of the x-ray examination, which disclosed the presence of enlarged bronchial lymph nodes.

W. A. H., male, aged twenty-nine years, a clerk by occupation, presented himself at the medical dispensary of the University Hospital on account of loss of weight (18 pounds), indigestion, and hoarseness when in the prone position. This latter symptom, which had been present for four weeks, was sometimes relieved by belching. He had no symptoms indicative of cardiac weakness. He had marked enlargement of the axillary lymph nodes and physical signs indicative of an infiltration of the left pulmonary apex.

Heart. Dulness extends from upper border of the third rib just below the right sternal border to one finger's breadth outside the midclavicular line. There is a marked presystolic thrill. On auscultation at the apex a rumbling presystolic sound is heard, ending in a loud booming systolic sound. The pulmonic second sound is greatly accentuated. The temporal arteries are sclerotic, the radial pulse has a small volume, that in the left being smaller than that on the right.

On further examination, an area of dulness above the heart and to the left of the sternum was discovered, which suggested the existence of an aortic aneurysm.

Laryngeal Examination (Dr. Singer). Complete paralysis of the left vocal cord, without any other signs of local abnormality.

X-ray Examination (Dr. Pancoast). The heart is enlarged after the manner indicated by the physical examination. The bronchial lymph nodes are enlarged.

Later on the patient developed cough when in the recumbent posture. The heart became more dilated, and the presystolic murmur less loud. About this time he became confined to bed,

his symptoms having progressively increased in severity. His private physician and a consultant, on being called to see him, pronounced his case one of thoracic aneurysm with cardiac enlargement. Death occurred as the result of edema, dyspnoea, etc. No autopsy was held.

Of all internal maladies, disease of the aorta is most frequently the cause of left recurrent laryngeal paralysis. Among 69 such cases Syllaba found 17, while Guder and Dufour encountered 8 cases among 79 (2 of complete paralysis and 6 of paresis) due to this cause. In 1 of Ortnier's and in 1 of Osler's cases aortic aneurysm had been diagnosed, and not unnaturally, since disease of the aorta and mitral stenosis may have many symptoms in common, among which inequality of the radial pulses and anisocoria,¹¹ cyanosis, cough, dyspnoea, aphonia, and pulsation in the second left intercostal space may be especially mentioned. Indeed, Boinet has suggested that periaortitis may cause a recurrent paralysis by direct extension without any compression whatever. It is also possible that antecedent infections, especially diphtheria, may give rise to the vocal paralysis. Chronic adhesive pericarditis, which was found in 3 of the reported cases, might readily account for the nerve paralysis. In Herrick's case the left recurrent laryngeal nerve was imbedded in a mass of cicatricial tissue.

The cases reported by Gantz and by Palasse were in all probability also the result of glandular pressure, a process in which it is incredible that the heart should have played any part. Pulmonary tuberculosis may cause recurrent paralysis either by direct glandular pressure—a gland is normally found between the bronchus anteriorly and the nerve posteriorly—or as the result of pleuritis, or through involvement of the pericardium or pulmonary consolidation. The knowledge of these facts makes one distinctly skeptical of the accuracy of Ceraulo's observations of twenty cases supposedly due to mitral stenosis. Quadrone reports eight cases in which paresis or paralysis of the cords occurred in cases of mitral disease, without any changes in the laryngeal mucosa, without any demonstrable cause other than the heart lesion. Three cases were examined with the x-rays. The reports of Syllaba, Alexander, Gavello, Quadrone, Perotta, Sheldon, Guder and Dufour, Pallasse, Pal, Ceraulo, Mead, Dmitrenko, and Koellreuter being unsubstantiated by autopsies, leave us in much uncertainty as to the actual mechanism of the compression, though they seem sufficient to emphasize the relationship of the two pathological conditions.

The observations of Ortnier to the effect that the pressure was exerted by the left auricle against the left bronchus in one case and against the aorta in the other, would seem to be faulty. To have the auricle press upon the aorta would necessitate that the pulmo-

¹¹ Harris, Harvein Society, London, 1903.

nary artery unguard the nerve by being thrust not only backward but downward and away from the aorta in a manner and to a degree that is practically inconceivable. As regards pressure upon the trachea by the auricle, it is anatomically impossible to have the recurrent laryngeal nipped between the left auricle and the bronchus. This statement is made despite the fact that both King and Friederich¹² have reported compression of the left bronchus by a dilated left auricle, an entirely different matter, and occurring below the lowest part of the recurrent laryngeal loop. These errors, like many others, tend to support the belief that the ordinary method of performing autopsies will not reveal the minutiae of interrelational thoracic anatomy. Only by having the body hardened before it is studied can such intimate details be determined with exact definiteness.

Kraus' explanation of the mechanism at work has more to commend it, although he is in error in regard to some of his anatomical relations. In addition to marked dilatation of the left auricle, he ascribes some of the trouble to a hypertrophied right ventricle, with consequent alteration of the relations at the aortic arch. He states that in his case the aortic ligament, instead of running upward and to the left, ran more horizontally. As a matter of fact, the abnormal course described by Kraus is the normal one. However, the ligament may have been more horizontal than usual, and this was probably caused by a pushing up of the pulmonary artery and not by a pulling down of the aorta.

In this connection it should be stated that the possibility of traction on the aorta by the pulmonary artery through the medium of the ligamentum arteriosum can hardly be looked upon seriously. The ligament runs antero-posteriorly and slightly upward, and before any downward traction could begin to be exerted the pulmonary artery would have to descend from 1 to 2 cm. It does seem a bit fanciful to assume that a structure but 2 to 3 mm. in diameter could pull downward the arch, supported as the latter is at both ends, and held up not only by the great vessels which arise from its convexity, but also by the attachment of the deep cervical fascia to the pericardium. These would certainly counteract any possible pull exerted by the ductus, to say nothing of the aid afforded by the areolar adhesions of the aorta to the adjacent mediastinal structures.

¹² Quoted Huchard, *Maladies du Cœur*, 1905, iii, 522.

TABULATION OF REPORTED CASES.

Observer.	Age.	Sex.	Cardiac lesion.	Autopsy findings: remarks.
Ortner, Wien. klin. Woch., 1897, No. 33	17	M	Double mitral and tricuspid; obliterative pericarditis	Nerve compressed between auricle and left bronchus; nerve discolored
	34	F	Double mitral and aortic; tricuspid insufficiency	Nerve compressed between left auricle and aorta; nerve flattened, constricted in spots and discolored
Herrick, Chicago Med. Recorder, 1898	38	M	Mitral stenosis; obliterative pericarditis and pleuritis	Nerve embedded in eieentricial tissue "and wedged between aorta and enormously enlarged left auricle that had forced its way in between the aorta and pulmonary artery considerably distorting the normal anatomical relations of the parts;" nerve flattened, narrow and attenuated and on microscopic examination was found degenerated; auricles greatly dilated.
Kraus, Verhandl. d. XIX. Kongr. f. inn. Med., 1901, p. 607	21	F	Double mitral; tricuspid insufficiency; slight aortic stenosis	Heart displaced by hypertrophied right ventricle, altering relationship of aorta, aortic ligament and pulmonary artery, with resulting traction on the nerve.
v. Schrötter, Zeit. f. klin. Med., 1901, p. 160	15	F	Double mitral, tricuspid insufficiency; patent ductus arteriosus; dilatation of pulmonary artery	Nerve compressed between origin of ductus arteriosus and aorta; constricted and discolored; trunk of pulmonary artery larger than ascending aorta, its two branches larger than normal; ductus arteriosus as large as the latter.
Hofbauer, Wien. klin. Woch., Oct. 9, 1902	32	M	Mitral stenosis	X-ray findings identical with those of Firscheuer; no autopsy.
Syballa, Sem. Méd., 1903, p. 44	47	M	Mitral stenosis	No autopsy.
Sheldon, Medical Rec., Nov., 1904	38	F	Mitral stenosis	No autopsy; vocal cord paralysis appeared and disappeared with broken compensation and improvement respectively.
Quadroni, "le paralisi delle corde vocali nei vizi mitralici," Seritti Medici in onore di C. Bozzolo, 1904, p. 515	..	F	Mitral stenosis and insufficiency	No autopsy notes; bilateral paresis; nerve histologically normal.
	..	F	Mitral stenosis	No autopsy; bilateral paresis.
	..	F	Mitral stenosis and insufficiency	No autopsy; bilateral paresis.
	..	F	Mitral stenosis and insufficiency	No autopsy; bilateral paresis.
	..	M	Mitral stenosis and insufficiency	No autopsy; bilateral paresis.
	..	F	Mitral stenosis	No autopsy; bilateral paresis.
	15	F	Mitral stenosis	No autopsy.
Alexander, Berlin klin. Woch., 1904, p. 135	..	F	Mitral stenosis and insufficiency	No autopsy; left rec. paralysis.
Firscheuer, Wien. klin. Woch., 1905, p. 1383	50	F	Mitral stenosis	X-ray findings identical with those of Firscheuer; no autopsy.
	30	F	Double mitral; tricuspid insufficiency	Nerve compressed between left pulmonary artery and aorta by forward and upward pressure of dilated left auricle and pulmonary vein.
Trétrop, Bull. de la Soc. belge d'otolaryngologie, 1905, p. 180	49	M	Mitral insufficiency	No autopsy; paralysis appeared and disappeared as patient got worse or better.
Hofbauer, Wien. med. Gesellsch., Nov. 14, 1905	30	M	Mitral stenosis	Nerve compressed between left auricular appendix and aorta, the former being pushed upward between the pulmonary artery and aorta.
Pal, Sem. Méd., 1905	No autopsy; brief verbal report.
Bonardi, Gazz. Med. Italian, 1906, p. 41	40	F	Double mitral tricuspid insufficiency; pericarditis	Nerve compressed between aorta and enormously dilated left auricle.
Koellreuter, Monatsch. f. Ohrenheilk., 1907, p. 1	29	F	No autopsy; x-ray, tracheoscopic, and esophagosopic examinations; mediastinal neoplasm; points out fallacy of accepting non-autopsied cases.

TABULATION OF REPORTED CASES—(Continued).

Observer.	Age.	Sex.	Cardiac lesion.	Autopsy findings: remarks.
Zimbler, Thèse de Balc, 1907	25	F	Congenital pulmonary stenosis and insufficiency; patulous ductus arteriosus	No autopsy; x-ray examination similar to that in v. Schrötter's case.
Gavello, Bull. di Malattie di Orechio, Nov., 1905	19	F	Mitral stenosis.	No autopsy; x-ray excluded possibility of disease of the aorta.
Ceraulo, Morgagni, 1907, No. 6	No autopsies; claims to have seen 20 cases in mitral disease, of which two were stenosis; no details.
Perotta, Arch. Ital. di Laryngolog., 1909, p. 71	38	F	Mitral stenosis	No autopsy; tertiary syphilis.
Guder and Dufour, Rev. de Méd., 1909, p. 300	43	F	Double mitral	No autopsy; partial paralysis; x-ray examination.
Osler, Arch. de Mal. du Cœur, 1909, p. 74	24	M	Double mitral	No autopsy; adhesive pericarditis?
	45	F	Mitral stenosis	Nerve compressed between left auricle and aorta?
	27	F	Double mitral	No autopsy.
	48	M	Double mitral with aortic insufficiency	Nerve compressed between left auricle and aorta. It was white and sclerotic; auricle size of small fist.
Boinet, Bull. de l'Acad. de Méd., 1910, p. 211	23	F	Mitral stenosis	No autopsy; paralysis appeared and disappeared as heart action became worse or better.
	25	F	Double mitral	No autopsy; x-ray showed great auricular dilatation, the aorta being apparently normal.
Pallase, Lyon Médicale, 1909, p. 719	20	F	Mitral stenosis	No autopsy; pulmonary tuberculosis; mediastinal adenitis revealed by x-ray.
Mead, Jour. Am. Med. Assoc., 1910, lv, 2205	..	F	Patulous ductus arteriosus; aortic and mitral stenosis; coronary and aortic sclerosis	Exact mechanism not stated; compression presumably due to dilatation of pulmonary artery which was distended to twice the size of the aorta; recurrent laryngeal nerve both macroscopically and microscopically normal.
Dmitrenko, Rousskyi, Vrach, 1910, No. 1; Abs. Arch. de Mal. du Cœur, Jan., 1911, p. 48	29	M	Mitral stenosis	No autopsy; paralysis attributed to dilatation of pulmonary artery; tracings were taken from same in the pulsating second left intercostal space; x-ray showed left auricular enlargement.

The obliterated ductus arteriosus is mentioned frequently in the autopsy records. It is our opinion that this structure is a factor of minor or even negligible importance, its main and perhaps only influence, aside from its mere presence, being to hold in approximation to a very slight degree the aorta and the left pulmonary artery. Even should the ductus be patulous, it does not follow that it has any intrinsic influence. We are inclined to believe that in these cases, such as v. Schrötter's and Mead's, the two factors of immediate significance are identical with those in which the ductus is obliterated, viz., the aorta and the left pulmonary artery, the patulousness of the ductus being of importance only on account of the associated dilatation of the pulmonary artery and the engorgement and hypertrophy of the right ventricle.

SUMMARY. There are now on record 11 autopsied and 26 clinically reported cases in which recurrent laryngeal paralysis was associated with and apparently the result of mitral stenosis. Among

the autopsied cases the vocal paralysis was attributed to direct compression on the part of the auricle or its appendix in 7; to cardiac displacement, traction, etc., in 1; to the effects of a persistently patulous ductus arteriosus in 2; and to indirect compression acting on the pulmonary artery in 2.

CONCLUSIONS. It is our conviction, based on careful study of the anatomical relations in hardened preparations, that the indirect mechanism may be a variable one, but that when compression is accountable for the recurrent paralysis, it must always be caused by the nerve being squeezed between the left pulmonary artery and the aorta or the aortic ligament.

Anything which will dilate or force upward the left auricle, the left upper pulmonary vein, or the left pulmonary artery would tend to cause the condition.

The anatomic relations are such that direct pressure of any portion of a dilated left auricle upon the aortic arch is impossible.

When we consider the softness of all the structures involved, and the fact that the nerve is normally flattened against the aorta, not rounded, it would seem probable that its function is abolished, not from actual destruction from pressure, but from a neuritis consequent upon a degree of compression which could hardly be sufficient to actually destroy the vitality of the nerve. This, of course, can be determined only by microscopic examination of the nerve.

ARNETH'S METHOD OF BLOOD COUNTING—ITS PROGNOSTIC VALUE IN PULMONARY TUBERCULOSIS.¹

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AND

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THE great difficulty of drawing a correct prognosis in a case of pulmonary tuberculosis is too well known to need more than a mention here.

Those most experienced in the treatment of this disease frequently fail to predict correctly the future course of a case, or to estimate with any degree of accuracy its chances of recovery. Therefore, any procedure which promises to be of assistance in drawing a prognosis demands our attention and study, and hence we feel justified in taking the time of this Association to present the conclusions we have formed from the study of the blood in a hundred cases of pulmonary tuberculosis by Arneth's method.

¹ Read before the American Climatological Association at Old Point, Va., June, 1909.

This method, developed by its author in Leube's clinic in 1904-05, has so far not attracted much attention in this country, though two of the members, of this Association, Dr. A. C. Klebs, and Dr. Geo. E. Bushnell, U. S. A., have made valuable contributions to the subject.

The former reported to the National Association for the Study and Prevention of Tuberculosis in 1906, and expressed the hope that his report might induce further investigation on these lines; but since that time, so far as we know, only Bushnell and Trueholtz have written on the subject.

Wishing to determine the value of this method as an aid to prognosis, we have examined the blood of somewhat over one hundred cases in Dr. Minor's practice, and as a result of this work we believe it has a distinct value in enabling one to estimate the resisting power, and hence the likelihood of recovery and general prognostic outlook, of such cases, and trust it will be more generally used by the profession than has been the case in the past.

As you all know, Arneth considered that the young white cells—those with one or two nuclei—are less resistant and less able to combat an infection than the older ones with more nuclei.

Starting out with this assumption, he counted the number of nuclei in all the neutrophilic white cells, and divided them into five classes, according to the number of their nuclei. Placing these numbers in a horizontal row, beginning on the left with Class I, which contained one nucleus, and ending on the right with Class V, which contained five nuclei, he formed what he called the neutrophilic blood picture. From a count of fifteen normal individuals he formed a normal picture.

I	II	III	IV	V
5 per cent.	35 per cent.	41 per cent.	17 per cent.	2 per cent.

Studying the blood in pulmonary tuberculosis, he found, in consonance with his theory, that the normal percentage of nuclei in the different classes was lost, there being an increase of the younger cells of Classes I and II, and a lessening of the more mature ones in Classes III, IV, and V, this being more marked in proportion to the severity of the trouble—one of the worst pictures he got being a case of miliary tuberculosis:

I	II	III	IV	V
36 per cent.	56 per cent.	8 per cent.	0 per cent.	0 per cent.

And again, in the case of subacute tuberculosis:

I	II	III	IV	V
45 per cent.	52 per cent.	3 per cent.	0 per cent.	0 per cent.

This change he calls a drift or dislocation (*Verschiebung*) to the left, and takes it as an evidence of a lowered resistance to the disease of the patient whose blood he is studying, as is demonstrated by the fact that, as the case improves, the picture tends to return to the right, and as it gets worse tends to move farther to the left.

With increasing experience with this method we have been more and more forced to believe that whether or not Arneth is right in his views as to the vitality of the neutrophiles of one or two nuclei, as compared with those of three, four, or five nuclei, the findings gotten by such counts agree remarkably well with the actual clinical facts, and that in his method we have a very useful means of drawing a prognosis in our cases of pulmonary tuberculosis.

Klebs and, especially, Bushnell² share this view, the latter believing that the drift is a proof that toxic absorption is present in a degree which constitutes a tax on the resistance of the patient.

In our cases we have found, with great but not complete uniformity, that favorable cases show a picture tending toward the right, unfavorable one tending toward the left, very much in proportion to the severity of the case and its outlook for a cure. In advanced and severe cases where, unfortunately, the prognosis is sufficiently evident, the picture is uniformly very bad, as in the following cases: The first, Mr. P. S., was from a very bad case of primary (?) pharyngeal tuberculosis with no pulmonary signs; the second, Mr. H. M. S., was a hopeless case of acute caseous pneumonia, grafted on an old chronic case; the third, Miss G., was a rapidly spreading acute tuberculosis, as was the third, Mrs. G.; while the fifth, Miss B., was an old chronic case with a large cavity in the upper left lobe, and an extensive infiltration in both lungs; while the last was a far advanced chronic case with extensive destruction.

	I	II	III	IV	V	Index.
(1)	41.5	43.5	10.0	2.0	93.0
(2)	34.0	45.0	20.0	1.0	89.0
(3)	39.0	47.0	14.0	93.0
(4)	48.0	42.0	8.0	2.0	94.0
(5)	54.0	36.0	10.0	95.0
(6)	55.0	42.0	3.0	98.5

But in much less advanced cases the method often gives us great assistance and throws unexpected light upon the future course. Not only would an unfavorable picture in a new case, which otherwise seemed fairly favorable, justify a strong suspicion of its outlook, but changes in the picture occurring during treatment can give us valuable hints.

Again, examinations during the course of a case, if not too close together, will generally show a drift to the right or to the left, according as the case is doing well or ill. In several cases we have found

² Loc. cit.

an unexpectedly bad picture, apparently not justified by the nature of the case, but whose reliability was only too well substantiated by subsequent developments.

TECHNIQUE. Coming to the technique of the procedure, we would first note that while it is more or less time consuming, it is not difficult to any one familiar with blood work. Our counts have all been done by Dr. Ringer in Dr. Minor's laboratory, with enough controls by Dr. Minor to determine the reliability of the system used. The blood was drawn from a free-flowing puncture in either the ear or the finger, and the resulting drop, which should be about 3 mm. in diameter, was touched to an underlying glass slide, previously washed in 95 per cent. alcohol to remove all fat. This drop was then evenly spread over the slide by slightly sweeping along it the smooth edge of the end of a second glass slide, held approximately at an angle of 45 degrees to the first. The spread must be made lightly to avoid deforming the leukocytes, and is allowed to dry in the air.

We found that the smears necessarily varied in thickness, and in the thicker portions that the leukocytes were smaller, the nuclei closer together, and often superimposed, so that an estimation of the actual number was very difficult; whereas in the thinner portions of the smear the leukocytes were not superimposed and were easy to count. Consequently the thin portions of the smear were always selected for the purpose of counting. To avoid counting the same cells more than once, a mechanical stage was always used.

We have used the Jenner stain in preference to others in our work; consequently allowing the smears to dry without fixation, and kept them in the staining fluid for five minutes.

We also stained smears with both Wright's blood stain and Ehrlich's tri-acid, but we found that Jenner's stain gave us the best nuclear differentiation, and consequently, we adopted this as a routine measure. Klebs, for similar reason, used Wright's stain, and Bushnell and Trueholtz, hematoxylin and eosin.

In every case we counted the nuclei, not of one hundred neutrophils, which Arneth thought sufficient, but of two hundred, and our percentages were estimated accordingly.

As in numerical blood counts each individual finally adopts a system of his own to which he adheres rigorously, so in this work we found it necessary to formulate certain arbitrary rules, which we have strictly followed, thus making our results comparable.

The chief difficulty has been to determine accurately how many nuclei a given leukocyte possesses, in order to be able to classify it correctly. Even in the thinner portions of the smear numbers of leukocytes will be found whose nuclei are not distinctly separated or only partially so; thus, the problem of correctly estimating the number becomes a very delicate one.

We have in all cases adhered unswervingly to the following rules:

1. Nuclei connected by a distinct isthmus are always to be counted as one nucleus.

2. Nuclei connected only by a thread are always to be considered as two nuclei.

3. Nuclei clearly superimposed are to be considered as separate nuclei, but if the superposition is not definite the nuclei are not to be considered as being separate.

Some may take issue with us as to the legitimacy of some of these rules, but we believe that the specific rule is of minor importance, the main point being that all counts be done by one and the same system, and preferably by the same individual, in order that the results may be really comparable.

As a result of our counts, done with every care, we have not been able to find a normal picture agreeing with that of Arneth, our normal, estimated in the case of ten healthy men, averaging:

I	II	III	IV	V
2.5	18.2	55.6	18.6	5.1

while our normal counts also show more cells from Class III onward, and fewer in Classes I and II, although Klebs, Bushnell and Trueholtz, and Webb and Williams, of Colorado Springs, who are to report shortly at the meeting of the American Medical Association, have agreed much more closely with Arneth. It is evident, therefore, that we have classed as multinuclear cells which they counted as mono- or bi-nuclear.

While we should like to have found ourselves in agreement with our colleagues, we can only repeat the facts as we found them, using, as we believe, the rational rules which we have quoted to guide us, and as the general relation of the pictures given by the different classes of cases is not thereby changed, as our tables show, we do not believe that the lack of agreement vitiates the conclusions we would draw from our counts, although unless the pictures be laid out in graphic curves, it renders it more difficult to compare the findings of different men.

Arneth, with characteristic German thoroughness, in classifying the nuclei has divided them even more minutely, and would distinguish in Class I between those with round nuclei and those with slightly and with deeply indented nuclei, the latter two being older; while in the other cases he separates the nuclei that are in loops from those that are round. Such an elaborate subdivision, while greatly increasing the complexity of the work, does not, we believe, bring compensating advantages, and we think, with Klebs and Bushnell, that it can be neglected.

Arneth lays stress on the fact that the drift to the left is independent of the total number of leukocytes, some people who present a normal leukocyte count showing a badly altered picture. In 33

per cent. of our cases we have made leukocyte counts, and have found this verified to a considerable degree, though, on the whole, the cases with the good pictures were usually those with lower leukocyte counts, while the bad cases usually showed the higher counts.

In our good cases the leukocytes averaged 7988, in our medium cases 9827, and in our bad cases 9258, and in one very bad case, 20,200.

It is evident that the comparison of different pictures, each with its five classes, will not be easy, and Arneth has taken the sum of the cells in Classes I and II to make a standard of comparison; while Bushnell and Trucholtz have sought to make an index for each case by adding together all the nuclei from Classes I and II and half of those in Class III, thus making the index the percentage of the lower half of the picture to the whole picture.

Thus, Arneth's normal picture would yield an average of 60.5 per cent., *i. e.*, 5×35 , $\frac{1}{2}$ of 41, while Bushnell and Trucholtz get 67, and Webb and Williams 65.

In our cases, since, as we noted, our Classes I and II show less cells, our index was lower, being 48.5 per cent.

While such an index is arbitrary, it is convenient for comparison in the investigation of our own cases, and unless something better is devised we would recommend its use.

At the same time, as already noted, for comparison between the counts of different authors a graphic chart should be plotted, as only in this way can the work of different men be compared. We would also state that there can be wide variations between maximum and minimum readings in each class of cases, our cases showing:

	Minimum.	Maximum.
Good cases	32.25	69 25
Medium cases.	38.0	70.5
Bad cases	61 5	87.0
Very bad cases	73.5	90.5

While Webb and Williams get:

	Minimum.	Maximum.
Normal cases	50	86
Cured cases	29	88
Improving cases	47	91
Stationary cases	31	94
Advancing cases	31	94

As we were studying the bearing of these counts on the prognosis of our cases we divided the hundred cases not according to the classification of Turban or the National Association, since certain Stage I cases can be severe or of bad outlook, while certain Stage III cases may be favorable and slow in course, but according to their clinical and prognostic outlook, classing them as good, medium,

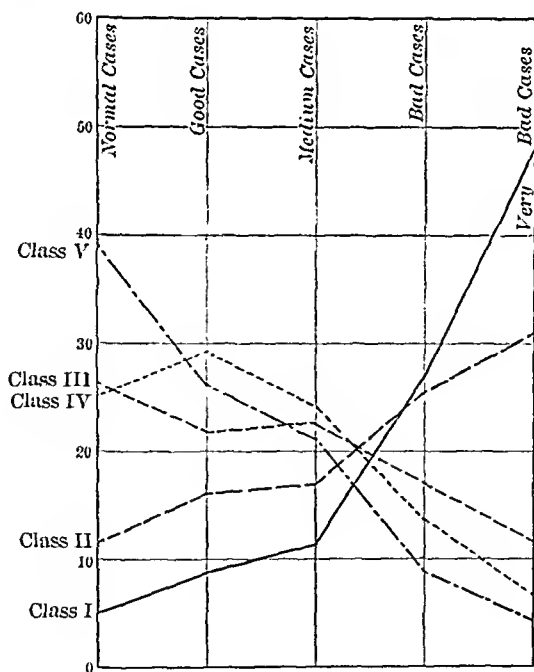
bad, and very bad, this classification being done by Dr. Minor from his knowledge of the cases without previous study of their counts, while Dr. Ringer, when he made the counts, took pains not to inform himself of the prognostic outlook of the cases.

Of course, the fault of this method is the personal equation which may enter into it, but for use in one's practice in studying one's cases prognostically this seems to us much the most practical division.

Webb and Williams have divided theirs into cured, improved, stationary, and advancing.

Tabulating our hundred cases in this way, we arranged them in four classes, and were surprised to find with what uniformity they bore out the contention of Arneth:

	I	II	III	IV	V	Average index.	Leuko-cytes.
Average of 10 normal cases . . .	2.5	18.0	56.0	19.0	4.5	48.5
Average of 31 good cases . . .	4.5	24.5	46.0	22.0	3.0	52.69	7988
Average of 30 medium cases . . .	5.5	25.5	48.0	18.5	2.5	54.85	9827
Average of 25 bad cases . . .	13.5	38.5	36.5	10.5	1.0	70.82	9258
Average of 14 very bad cases . . .	24.0	45.5	25.0	5.0	0.5	88.03	20,200



Relative position and change in each group.

A glance at this chart, which, as I have said, was not forced in any way, will surprise one by the regularity with which, in Classes I and II, the figures rise through the light cases to the very bad; how in Class III there is a much slighter rise; while in Classes IV

and V there is, on the contrary, a fall, the general increase in the lower classes being well shown by the index.

This is made even more apparent when these are plotted out in graphic curves.

A study of these tables certainly seems to justify the belief that the discovery of a distinctly poor picture in a case can have real prognostic value, and that even when the clinical course of the case seems favorable a bad picture should cause us to look out for unfavorable developments.

Thus, in one of our cases, a young man (Mr. W. B.), who, as already noted, seemed to be doing well, we were surprised to find a picture:

I	II	III	IV	V	Index
20	45	30	5	0	80

unexplainable by the apparently satisfactory state of the case, but which was shortly followed by a severe exacerbation of the trouble which spread rapidly and ended fatally in a few months. One month from the first reading we found:

I	II	III	IV	V	Index
38.5	49.5	10.5	1.5	93.5

It must, however, be carefully noted that small variations should not be considered of value, and that there must be distinct changes before we proceed to draw conclusions from them.

In old cases a study of the picture over a series of months will usually show a rise or fall of the index according as the case is running down or up hill, but in any given case we should not expect notable changes under two or three months, unless, as in the case cited just before, there is a rapid extension, or unless a severe hemorrhage occurs, when naturally the number of newly formed leukocytes is increased.

Thus, in one severe case (J. M. H.) we found on December 4, 1908:

I	II	III	IV	V	Index
15.0	50.0	22.5	11.5	1.0	76.25

And on February 11, 1909, just after a large hemorrhage:

I	II	III	IV	V	Index
33.5	50.5	13.0	3.0	0	90.5

while, though he continued to go down hill, on March 26, 1909, he showed:

I	II	III	IV	V	Index
27.0	49.5	20.5	3.0	0	86.75

thus showing that the hemorrhage, by causing a formation of many new leukocytes, had artificially raised his index.

The rapid deterioration which can occur in a severe case is well shown in readings only a month apart in the case of caseous pneumonia we referred to earlier (H. M. S.). Here, on March 2, 1909, we found:

I	II	III	IV	V	Index
15.0	40.0	40.0	5.0	0	75.0

while on April 5, 1909, we found:

I	II	III	IV	V	Index
34.0	45.0	20.0	1.0	0	89.0

In a severe case with general dissemination over both lungs (E. H.), which after a long course and the greatest care was slowly recovering his health and has since gone home "arrested," we were unfortunately not using this method on his arrival, February 27, 1908; but on December 1, 1908, when he was in very good condition, but by no means in the excellent shape he showed on discharge, we found:

I	II	III	IV	V	Index
10.5	35.5	35.5	17.5	1.0	73.7

while on May 29, 1909, shortly before his return to Chicago, we found:

I	II	III	IV	V	Index
5.0	34.0	50.0	11.0	0	64.0

Again, in a severe case of chronic tuberculosis with great prostration and much active tissue destruction in the lungs (I. W. S.), he showed on March 18, 1909:

I	II	III	IV	V	Index
32.5	47.0	16.5	4.0	0	87.75

while, after very satisfactory though slow improvement, with increased weight and appetite, markedly decreased fever, cough and expectoration, and great improvement in the physical condition of the lungs, he showed, on May 26, 1909:

I	II	III	IV	V	Index
18.0	48.5	28.5	5	0	80.75

a relatively slight change, but one which, viewed in connection with his clinical improvement, distinctly increased our hopes of final betterment.

Again we will find cases which, despite good gains, show a rising index, and here we have come to feel that such a rise detracts greatly from the meaning of such improvement. Thus, in a severe case with bad pulmonary, laryngeal, and probably intestinal lesions, the patient made considerable gain. The laryngeal trouble was less active, the diarrhoea ceased, and while the physical findings in the lungs only moderately improved, the symptoms did. Nevertheless, on November 26, 1908, this case (M. L. D.) showed:

I	II	III	IV	V	Index
14.0	50.0	30.5	5.5	0	79.2

and on December 29, 1908:

I	II	III	IV	V	Index
24.0	49.0	24.5	2.5	0	85.2

and the course of this case since that time, though another count has not been made, would seem to indicate that the index was a reliable guide.

Again, a pulmonary and laryngeal case (M. N. G.), which for some time gained weight and made some improvement, but has not held these gains in the last month or so, showed, on November 24, 1908:

I	II	III	IV	V	Index
10.0	43.5	35.0	11.5	0	71.0

and on January 8, 1909, although she seemed to be still doing well:

I	II	III	IV	V	Index
13.5	43.5	36.5	5.0	1.5	75.25

We could cite many more pictures, were it necessary, which would show the utility of this method of counting the blood, but we believe we have presented enough to make this clear.

While it is far from infallible, it is nevertheless a distinctly valuable guide in the formation of a prognosis, though as we have tried to show, it will not do to draw large conclusions from slight variations in the blood pictures, either from month to month or at first examination.

Like every other method of clinical medicine, it should be used conservatively and judiciously, but if so used we feel that it will prove a valuable addition to our clinical methods.

Nearly two years have elapsed since the above paper was written,

and we have had ample opportunity to test the matter further, and have used it in nearly 500 cases. As a result of this work we are more than ever satisfied of the correctness of the conclusions we drew at that time.

A few cases may here be cited among many that we have examined:

In April 17, 1909, H. A., a second-stage case, after some months of cure was doing remarkably well, had lost all constitutional symptoms, cough and expectoration were slight, weight excellent, and general outlook good. At this time his blood read:

I	II	III	IV	V	Index
4	16	48	30	2	44

Since this time family troubles and financial difficulties necessitated hard work beyond his strength; he has been steadily running down hill; the lesions in his lungs have increased; the larynx is seriously involved, and the outlook we consider bad. On March 11, 1911, we found:

I	II	III	IV	V	Index
41	41	17	1	0	90.5

On the other hand, M. J. E., on arrival, March 11, 1910, had a severe and active process, chiefly in left lung, and showed:

I	II	III	IV	V	Index
25	54	19	1	0	89.5

He made rapid and remarkable gains, and by July 1, 1910, he showed:

I	II	III	IV	V	Index
12	40	41	6	1	72.5

while now (March 15, 1911) his process is arrested and his reading is:

I	II	III	IV	V	Index
2	37	54	7	0	66

I. N. R., a medical student, arrived March 17, 1909, with an active bilateral process with tendency to frequent "congestions." At that time his reading was:

I	II	III	IV	V	Index
27	46	19	8	0	82.5

With care, by May 19, 1910, all activity had ceased and he was classed "apparently cured," a condition which has since continued. He then showed:

I	II	III	IV	V	Index
3	38	48	10	1	65

Miss M. G. G. arrived June, 1910, with a very acute process, with high fever, marked symptoms, and a diffuse involvement of

her right lung, with a very grave prognosis. July 20, 1910, her reading was:

I	II	III	IV	V	Index
18	56	26	0	0	87

November 22, 1910, after four months of unexpectedly favorable progress, with symptoms greatly reduced and signs improving, she showed:

I	II	III	IV	V	Index
8	39	41	11	1	67.5

and went home apparently cured March, 1911. Unfortunately, a last blood count was not made.

• Mr. E. S. T. had done very well, and after six months of care showed, May 14, 1910:

I	II	III	IV	V	Index
8	28	52	12	0	62

Returning home to great business anxiety and overwork, he later developed laryngeal trouble, and on return, November 28, 1910, showed:

I	II	III	IV	V	Index
9	49	39	8	0	72.5

These are but a few of the cases that have caused us to rely on this method for aid in drawing our prognosis and justify us in recommending it to the profession.

There have been cases in which it has failed us, but there have been very many, the large majority of all those seen, in which it has been of distinct value, and where the course of the case has verified the predictions of this method.

SOME EXPERIENCES WITH THE EINHORN DUODENAL BUCKET AND A MODIFIED THREAD TEST.¹

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IN April, 1909, Dr. Max Einhorn described the use of his duodenal bucket and the thread impregnation test as an aid to the diagnosis of, and as a means for the location of, peptic ulcers. Shortly afterward I employed this procedure in several cases, but later adopted a modification in place of the bucket, which I will describe.

¹ Read before the American Gastro-Enterological Association at St. Louis, June 6, 1910.

MORGAN: THE EINHORN DUODENAL BUCKET

No.	Date.	Name.	Hematemesis.	Benzidine.	Brown stain.	Distance from mouth.	Position.	Remarks.
1(a) (b) (c) (d)	November 9, 1908 November 11, 1908 December 23, 1908 October 23, 1909	Mr. R. N. J.	No	Onco only	++ ++ +	43 to 54 cm. 50 to 57 cm.	Lesser curvature	4 tests made. (c) Much less and lighter than others. (d) After nearly one year. Most probably ulcer.
2	March 5, 1909	Miss L. G.	No	Not made	0 2 stains	56 to 57	Pylorus and duodenum	
3(a) (b)	October 12, 1909 December 19, 1909	Mr. G.	No	+	+	58 to 70	Pylorus	(a) Test made just before operation. (b) After gastro-enterostomy one month.
4	October 30, 1909	Miss M. T.	Slight (1)	Negative	0	More likely gall-bladder than ulcer.
5	Mr. C. S. W. T.	No	++	2 stains	40 to 48	Lesser curvature	Symptoms were only suspicious of ulcer.
6	December 9, 1909	Miss C. C.	No	Trace	+	61 to 71	Duodenum	Moderately well-marked ulcer symptoms with colitis.
7(a) (b)	December 9, 1909 December 12, 1909	Mrs. J. B. W.	No	Negative	++	42.5 to 43.5 41 to 42	Cardia	Symptoms of ulcer and gallstones.
8	December 9, 1909	Mrs. W. S. H.	No	Not made	+	46 to 48	Lesser curvature	Epigastric pain, acid stomach, tender spot.
9(a) (b)	December 15, 1909 December 16, 1909	Mr. G. H.	No	Trace	0 +	43 to 47	Lesser curvature	First test negative for some unknown reason.
10	December 13, 1909	Mr. H.	No	Not made	0	Nervous dyspepsia. Pain and burning in pit of stomach.
11	December 6, 1909	Mr. P. J. Me.	No	Not made	0	Questionable ulcer of stomach.

12	December 22, 1909	Miss B.	+	+	+	+	+	35 to 72	Stomach filled with blood	Operation showed indurated ulcer of pylorus and lesser curvature.
13	December 23, 1909	Miss P.	No		Negative	0	Probably ulcer on posterior sur- face.
14	December 23, 1909	Mr. A. L.	No		Negative	0	Hyperacidity relieved by treat- ment.
15	December 29, 1909	Mrs. T. H.	No	+	+	+	Very faint	63 cm.	Duodenal	Able to keep bucket down but one hour.
16	Mr. D.	?	+	+	0	Duodenal	Operation showed duodenal ulcer five inches down.
17	Mrs. S.	No		Negative	0	Auto-intoxication.
18	January 24, 1910	Mrs. B.	No		Negative	Small spot	49 cm.	...	Lesser curvature	Had pain only when shot was in situ.
19	January 26, 1910	Mr. G. D. D.	No		Not made	+	60 cm.	...	Duodenal	Suspicious symptoms only.
20	January 22, 1910	Miss K. A. D.	No		Not made	0	Gall-bladder symptoms.
21(a)	May 8, 1910	Miss W. S. W.	Good many	+	+	+	2 spots	(a) 43 to 45 cm. 62 to 63	Lesser curvature	(b) After ulcer treatment for one week.
(b)	May 15, 1910					2 spots	64 to 65	
22	May 12, 1910	Mr. D.	No		Negative	Slight	54 to 56 cm.	...	Pylorus	Certain ulcer, perhaps cancer superimposed.
23	May 11, 1910	Capt. O.	No		Negative	0	Hyperacidity.
24	May 15, 1910	Mr. B.	No		Not made	+	55 to 56	...	Pylorus	
25	May 15, 1910	Mr. S.	No		Negative	0	

A split BB shot is fastened to the end of a No. 8 braided silk thread. The shot is enclosed in a 5-grain capsule, the cord passing through a small hole in one end; 75 cm. from the capsule a knot is made.

The manner of using the duodenal shot is the same as that for the bucket. For several hours before beginning the test, medicines which may discolor the thread are discontinued, and for supper no meat should be allowed, the meal preferably consisting of milk, eggs, bread, and butter. At bedtime the patient swallows the capsule and thread until the knot is at the teeth. The end of the string is then made into a loop and fastened to the nightgown with a safety pin, so that the knot just remains in place. The shot remains down all night, in the meantime passing through the pylorus. On awakening, the patient pulls the thread out and hangs it up to dry, being careful not to allow any thing to touch it while wet. Inspection of the dried thread shows the lower end bile stained where it has remained in the duodenum, and if blood is present it is indicated by a reddish-brown discoloration.

The principal advantage of the shot over the bucket lies in its cheapness. Any number of the tests may be carried on at one time, whereas we do not usually possess more than one bucket set. Again, somewhat more ease is experienced in swallowing the smaller capsule, and the removal is decidedly facilitated. There is no obstruction whatever felt in drawing up the small shot, it not even being necessary to swallow when the base of the tongue is reached. But the shot has the disadvantage of not being hollow, and we cannot, therefore, obtain any of the fluid to determine whether or not in a doubtful case the end of the thread entered the duodenum. Another disadvantage is that by means of the bucket we can determine whether or not the pylorus is normally permeable.

At first I used the thread impregnation test rather spasmodically, but for the past several months have employed it more systematically in cases of suspected ulcer. I have taken from my records 25 cases upon which I have performed the test thirty-two times. The results are shown in the accompanying table (pages 650 and 651.)

Of the cases cited, 16 were undoubtedly ulcer—Nos. 1, 3, 5, 6, 7, 8, 9, 12, 13, 15, 16, 18, 19, 21, 22, 24; 3 cases were suspicious—Nos. 2, 11, and 4; cases certainly not ulcer were Nos. 10, 14, 17, 20, 23, 25.

Of the 16 ulcer patients, the thread test gave positive results in 14 and negative in 2. These 2 negative results can both be accounted for theoretically. No. 13 had ulcer symptoms beyond doubt, and recovered under ulcer treatment, but since no mark appeared on the thread, and no spot of tenderness could be elicited, I judge that the lesion was on the posterior surface of the stomach. The other patient, No. 16, was proved by operation to have a duodenal

ulcer 3 cm. from the pylorus, and in all probability the shot came to rest just above the lesion.

Of the suspicious cases, No. 2 gave a positive reaction, showing two spots, due to a pyloric lesion. The diagnosis was never confirmed, but an ulcer was undoubtedly present. She was a young woman, aged twenty-five years, who had attacks of abdominal pain somewhat localized in the epigastrium, accompanied by intense nausea and vomiting. Often food remained in the stomach six to eight hours undigested. Vomiting rarely continued after all food had been expelled. Often water was rejected. After the attack passed off the abdomen was very tender, but the tenderness was not well localized. She had a temperature of 102° to 104° during attacks, and in one was delirious. Often before the attack the skin had a subicteroid hue, but jaundice was never present.

Patient No. 4 had practically no ulcer symptoms, but had a history of slight hematemesis some time before. Was very anemic. Hemoglobin, 45 per cent.; had pains in the epigastrium, which, however, were much like those of gall-bladder disease, and the tenderness was over the gall-bladder. Attacks of diarrhoea were the chief complaint. The blood at no time indicated pernicious anemia. The duodenal bucket was introduced at 9 P.M. and removed at 3 A.M. Thread showed no blood stain.

The third questionable case was No. 11. The patient complained of continuous pain in the stomach influenced by the character of food. No vomiting, but some nausea. Hyperacidity but no particularly tender spots. The thread test was negative. I have always felt that this man had an ulcer, and he improved steadily under ulcer treatment.

Of the undoubtedly non-ulcer cases, the following were tested: Nervous dyspepsia and hyperacidity, each 2 cases; auto-intoxication, gall-bladder disease, and stenosis of the gall-bladder, each 1 case. None gave a positive thread test. I have not made use of this method of diagnosis in gastric carcinoma, so none of these cases appear in the table.

Operation was performed on but 4 of my patients. The diagnosis was corroborated in cases 1, 3, and 12. No. 7 was operated upon for gallstone, but no adequate examination for ulcer was made at the operation. Her record will be given in detail below.

Repetition of the test was made in several patients and with the exception of No. 9 the findings were identical when the patient's condition was the same as at the previous examination. The first test in Case 9 was negative for some unknown reason, but a second attempt on the following day showed a well-marked stain 43 to 47 cm. from the mouth.

I feel that the thread test is a valuable addition to our armamentarium in the diagnosis of gastric and duodenal ulcer. I was somewhat surprised at the scarcity of the so-called cardinal symptoms

in my series, and several of the patients would, without this test, most likely have gone with their ulcers unrecognized at least for several months until resistance to other treatment would have called attention to the true state of affairs.

It is, I think, significant that not only did hematemesis occur but three times, but that even vomiting was absent in the majority of patients, unless of the induced variety. Tenderness was absent throughout, or present only at intervals in the course of many cases. The character and time of the pain varied greatly.

The benzidine test for occult blood in the stools was performed in 13 of the cases showing positive thread tests. It was positive in 9, and negative in 4. It seems to be not so delicate or constant as the thread test.

In the differential diagnosis between ulcer and gall-bladder disease the thread test is very valuable. I may mention 3 cases: No. 7 had both conditions; No. 15 had ulcer, but no gallstones, though symptoms were suspicious of the latter; No. 20 had cholecystitis and no ulcer. I will report the first of them rather fully because it was an exceedingly interesting one to me, but as the record is a very long one, covering a year's time, it will have to be considerably abridged.

Mrs. J. B. W., married, four children, seen December 9, 1909. Family and past history unimportant. Illness is of ten years' duration, starting gradually and pursuing an irregular course. Had attacks of acute severe cramping pains in stomach just below xyphoid referred to the chest and back under the shoulder blades. Often had attacks between the hours of 2 A.M. and 3 A.M. Had heart-burn and pyrosis, relieved for a time by food. Some regurgitation was present. Belching was annoying after lunch and dinner. The bowel actions were irregular. Had abdominal pain sometimes before a loose movement. The principal points of the abdominal examination were: Right kidney palpable to first degree, left not palpable. Panniculus good, belly well formed. Splashing sound all over epigastrium down to navel. No tender spots. Some meteorism. Gall-bladder flaccid, easily felt, and not tender. Blood pressure, 108 mm. One hour after test meal were recovered 60 c.c. of a greenish-yellow fluid, acid, food particles coarse. Mucus present. No blood or tissue. Bile present. Free HCl, 42. Total acidity, 68. A later examination gave free HCl, 60; total acidity, 90. The patient was put on ulcer treatment for a couple of months and steadily improved until February, 1909, when she became worse. Stomach was very hyperesthetic and she had constant pain. For the next ten months patient was alternately better and worse—sometimes apparent ulcer and sometimes gallstone symptoms supervening. She was under the observation of Dr. Howard Kelly for four days, and no diagnosis was made. On December 10, 1909, the duodenal shot test was made, and showed bright blood

stain in region of pylorus. The lower 8 cm. were deeply bile stained. January 5, 1910, operation was performed by Dr. A. L. Stavely. The gall-bladder was tense and contained two ounces of changed black thick bile and mucus. A stone the size of a nutmeg was found engorged in the cystic duct and removed. No adequate examination of the stomach was made to determine the presence of an ulcer, but there is no doubt as to its existence. The case then passed from my observation, so I cannot say as to the present status.

According to the method of localization given by Dr. Einhorn, a spot at the distance of 40 cm. from the mouth indicates ulcer of the cardia, 44 to 54 cm. of the lesser curvature, 56 to 58 cm. of the pylorus, and above 59 of the duodenum.

Of my series, the cardia was involved in 1 case; the lesser curvature, 5 cases; pylorus, 3 cases; duodenum, 4 cases; pylorus and lesser curvature, pylorus and duodenum, and lesser curvature and duodenum, each 1 case.

In patients whose stomach contains much blood or in whom blood is regurgitated from the duodenum through the pylorus it is impossible to localize the ulcer by the thread, as, of course, a large discoloration occurs. Two or more stains upon the same thread do not usually indicate a multiple lesion, since in its passage through the viscus different portions may come to rest over the ulcer. Such was my experience in 3 of the series. Under favorable ulcer treatment and after hemorrhage has been diminished, a later test will probably give more accurate readings.

This leads me to speak of the test as a means of judging the progress or apparent cure of a case. Illustrating this, I will cite Cases 1, 3, and 21.

A synopsis of No. 3 follows: It is of interest in that the questionable diagnosis of ulcer was clinched by the thread findings, and a correct localization made as afterward proved by operation. Again, the second test showed the cure of the lesion following gastroenterostomy. Mr. C. W. G., single; aged twenty-seven years; electrician; nervous temperament. Seen July 18, 1909. Trouble of four or five years' duration off and on. Gradual onset with mild symptoms. Might have freedom from pain for months and then have symptoms for two weeks. Pain across abdomen in region of navel, passing up under right costal border. Often came on at night. Food sometimes relieved and again aggravated, but, as a rule, he was afraid to eat during attacks. Pyrosis, but no recent heartburn. Complained of bloating and feeling of fulness. No nausea, no involuntary vomiting.

Principal points of the abdominal examination were: Recti slightly resistant. Some tenderness of the transverse colon throughout its course. Excessive meteorism. Splashing sound all over epigastrium down to navel. Hemoglobin, 102 per cent. Blood pressure, 106 mm. Stomach contents an hour after test breakfast

showed 100 c.c. cream-colored, acid fluid, containing fine food particles. Mucus absent. No blood, tissue, or bile. Free acid, 44. Total acidity, 88.

Patient was put on the usual treatment for hypersecretion, frequent meals, baths, magnesia p. c., and kept under observation. One week later the pain became somewhat more localized, coming on several hours after meals. For next two months he was for the most part better, but had several attacks of pain. He went on his vacation. At first he did well, but after a time had an acute severe attack with the only vomiting he had at any time. Lavage showed no retention.

Three days later he was sent to Garfield Hospital. After starving him for twenty-four hours, gradual feeding with milk was begun. As soon as diet would be increased he had return of pain—coming on principally at 4 P.M. and 10 P.M. Examination rarely elicited much tenderness. October 27, 1909, Dr. L. H. Reichelderfer saw him in consultation, but the examination was so negative that he did not advise operation at that time. His condition remained about the same for two months more, when Dr. Thos. Kelly saw him. He thought that there was a strong probability of ulcer or gallstones, and advised exploratory operation. Deep pressure caused resistance of the right rectus and slight muscular spasm. At this time examination of his stool showed occult blood present for the first time. October 12, 1909, the duodenal bucket was given at 9 P.M. and removed the next morning just before etherization. The thread had tangled into a knot, so that it was shortened about $2\frac{1}{2}$ inches. It had passed the pylorus, however, and showed a definite blood stain at that place. Operation by Dr. Kelly disclosed a large mass the size of an egg at the pylorus—a saddle-shaped ulcer. Posterior gastro-enterostomy was performed. Recovery was uneventful excepting for considerable nausea and the passage of a moderate-sized tarry stool three days after operation. The patient gained twenty-five pounds, and a second thread test two months later was negative.

I shall also quote case No. 1 as illustrating two points—(1) the disappearance of the stain from the thread when the ulcer has healed, and (2) the discomfort and occasional actual pain which is sometimes encountered when the bucket is in situ. Mr. R. N. J., aged thirty-two years, clerk. Family and past history unimportant. Illness of sudden onset two months previously, with pain just below the xyphoid, not distinctly localized. Almost constant pain, but relieved by food for a couple of hours. Gas formation with much belching. Slight nausea, but never vomiting. No appetite. Bowel movements consisted of hard lumps in liquid content. Had lost thirty pounds since onset. Moderate tenderness on deep pressure over entire epigastrium, but more marked at a circumscribed spot about one inch in diameter one inch above navel. Slight tender-

ness over entire colon. No meteorism. Splashing sound over entire epigastrium to navel. Physical signs otherwise unimportant. Blood pressure, 120 mm. Hemoglobin, 98 per cent. One hour after test breakfast stomach contents showed 25 c.c. of a cream-colored fluid, acid, with fine food particles. No mucus, blood, or tissue. Bile, a trace. Free HCl, 26. Total acidity, 38.

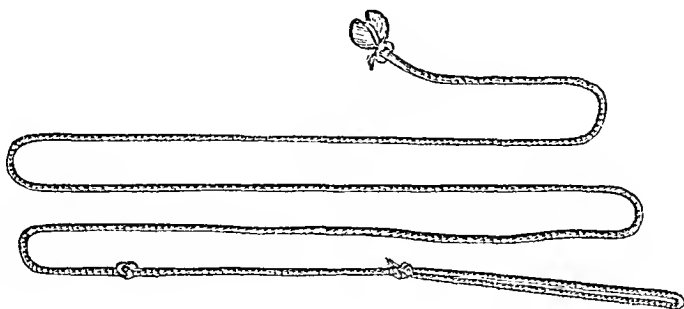


FIG. 1.—Negative thread. Miss K. H., May 25, 1910.

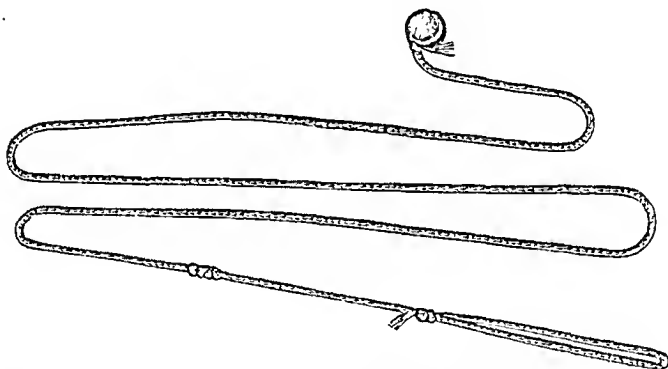


FIG. 2.—Well-marked stain 55 to 56 cm. from mouth; undoubted ulcer; improving steadily under treatment. Mr. J. B. J.; test made May 24, 1910, after paper was written.

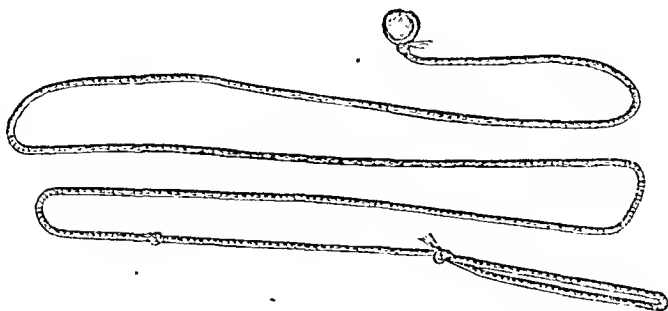


FIG. 3.—Thread showing presence of much blood in stomach. Mrs. R.; test made June 2, 1910.

He took the duodenal bucket at 9.30 P.M., and felt uncomfortable as soon as it was in the stomach, having slight nausea and

considerable pain in upper left portion of abdomen. Went to sleep about eleven o'clock but awoke about 3 A.M. with paroxysms of pain, which would come on in waves and seem to pass from left to right. Had a feeling of constriction under the xyphoid. Removed the thread at 6.30 A.M. Considerable bright blood and some dark blood stains were present. Several other times the test was made, and each time the stains were the same, and he had the same symptoms while the bucket was in situ.

May 22, 1909, after having been in bed for some weeks and treated for ulcer, he was apparently cured. For the next year the patient had varied symptoms referable to his stomach and bowels, acute attacks of hyperacidity, and some pains. At one time there was slight retention, so that it was feared that the old ulcer cicatrix had contracted. The thread test performed again shortly after this showed absolutely no evidence of blood.

Another case, No. 21, shows the improvement, as mentioned by Dr. Einhorn, which may occur in a week's time after regulating the diet. Test (a) May 8, 1910, showed two well-marked stains, one at the position of the lesser curvature, and the other at the duodenum. One week later, May 15, 1910, the same two stains appeared, but so faint as to be just perceptible. In such rare instances as this we may consider the possibility of a multiple lesion.

The performance of the thread test is in rare instances somewhat disagreeable, and has produced actual pain in two cases—Nos. 1 and 12. No. 15 was able to keep the bucket down only an hour, but even this short time sufficed to localize the ulcer by a faint stain. Fortunately the majority of patients do not object to the test, and I should strongly recommend that it be more generally used in all cases of severe pain in the stomach.

In conclusion, I would say that the thread test, whether performed with the Einhorn bucket or the duodenal shot, is of undoubted assistance in the diagnosis of peptic ulcer. The number of latent ulcers, or ulcers having few prominent symptoms, is larger than is generally thought, and by the systematic use of the thread test many cases will be found that would otherwise escape recognition. The test, though sometimes disagreeable, is not seriously objected to, and should be instituted on the faintest suspicion of ulcer. Finally, besides being able to localize the lesion, we are enabled to say with more certainty how the case is progressing and when the ulcer is probably cured.

RESEARCHES IN PROPHYLACTIC AND ANAPHYLACTIC MEDICINE.

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THE first work produced in our country upon the important subject of anaphylaxis was by M. J. Rosenau and John F. Anderson in the Government Hygienic Laboratories in Washington. It is superfluous to add that I, and all of us, are now, as we have been ever since 1906, very much dependent upon these two prolific investigations for most of the suggestive work on this subject.

The Greek words, *ἀνὰ* meaning against, and *φύλαξ* guard, give us the word *φύλαξις*, which is the origin of prophylaxis or protection. Charles Richet, who, in 1902, while investigating actinia poisoning, first observed a condition in dogs, which he considered a reduction of resistance, as contrasted with prophylaxis, invented the name anaphylaxis. Although this name has been adopted and passed into medical usage, the kind of protoplasmic reaction it includes, is one of the various progressive steps the organism makes in many infections in obtaining for itself protection or immunity. This view of anaphylaxis may now be taken without fear of a dissenting voice. That prophylaxis is the follower and slave of anaphylaxis will be proved subsequently by various examples. It is only necessary here to mention the reaction of the human organism to the vaccines of cowpox.

The latent period between the abrasion inoculation and the primary reaction in a first vaccination is four days, with sharp clinical signs. Each subsequent vaccination has a reduced latent period. Relapses in typhoid fever may also be cited, as well as the autumnal-spring return of those infected with tertian and quartan fevers. Hay fever and tuberculin reactions are other examples.

Clemens von Pirquet first suggested that prophylaxis, anaphylaxis, immunity, and other tissue reactions yet to be discovered, should all be covered by his coined name, viz., allergic or allergism. This is also from two Greek roots, *ergon* action, and *allos*, change.

Allergie is comprehensive enough to include all conditions of artificial immunity, with or without anaphylaxis. When there is an increased allergie, it means that the power of the tissues to react is increased, and this plainly indicates hypersusceptibility or a condition of anaphylaxis.

In the unexpurgated edition of his diary Pepys, who lived at the court of Charles II, tells that the blood of a dog is poisonous when injected into another animal. He describes several trans-

fusion experiments. Since then it has not passed unrecognized by many observers, that the serum of one species is occasionally toxic when inoculated into the animals of another. It has also been long known that the horse, pony, and donkey serum, could with impunity be inoculated in quantities into many species of animals.

Yet long before von Pirquet classified the "serum disease," the symptoms had been reported by various internists following antitoxin injections. The case of Pettenkofer's child in Berlin, whose sudden death in 1899 was ascribed to diphtheria antitoxin, and later blamed on that misty malady "status lymphaticus" is now recalled, and ascribed to the "serum disease."

In the latter part of August, 1910, W. L. Moss, of the Johns Hopkins Hospital, calls attention to certain anaphylactic skin manifestations. He suggests that 0.01 c.c. of normal horse serum preserved with a few drops of chloroform be injected into the skin. If an area of inflammation appears within twenty-four hours it is an indication that the individual has received horse serum (antitoxin) at some previous period, although a negative reaction does not necessarily exclude that fact. If the protective reactions appear with "explosive suddenness" and immense wheals of an urticarial nature are exhibited within ten hours, it is an indication of latent anaphylaxis.

The erythemas, urticarial manifestations, swollen glands, joint effusions, intramuscular œdema, pain and fever of von Pirquet's disease may be easily diagnosticated if Moss' test is confirmed. The seven to fourteen day incubation period, need not then delay treatment or the diagnoses.

Though egg albumin, milk, or, in short, any protein will by inoculation produce the phenomena of anaphylaxis, the proteins of horse serum are so closely associated with the greater part of the work and with modern therapy that most of the history and present knowledge of hypersensitiveness deals with that serum.

Although Pepys reported in newspaper fashion certain hearsay cases of transfusion, Magendie, in 1839, tells of rabbits that died from a third inoculation of egg white. Arloing opined in 1888 that bacteria send out toxins that reduce the resistance to further infection. Knorr, working in 1895, with tetanus toxins, blamed the latter, when sublethal doses were injected in increasing doses, for the death of the inoculated guinea-pigs.

In 1897, Uhlenhuth first produced anaphylactic states in guinea-pigs, but failed to recognize the cause of death. He used the blood of six species, including man, for his blood-inoculation experiments. Courmont, in 1900, was the first to ascribe the death of guinea-pigs to repeatedly smaller injections of human serous fluids. The following year von Behring and Kitashimia used the word "hypersusceptibility," but blamed it upon the bacterial

toxins, not proteins. Then Portier and Richet hit on the real word as described above. Arthus, in 1903, brought the subject of anaphylaxis almost up to date. Rosenau and Anderson's early work was in part a confirmation of Arthus'.

Von Pirquet, in 1903, announced the clinical signs and symptoms of the serum disease. If a guinea-pig is given 0.001 c.c. of horse serum, and two weeks afterward another injection larger than the first, death will inevitably ensue.

When Professor Paul Ehrlich was in Boston in 1904, Theobald Smith related this fact about guinea-pigs that had been used for standardizing antitoxins. Ehrlich could not explain it, but suggested to an assistant, Otto, that he work it out. Otto excluded the antitoxin as a cause, and called the manifestation a "Theobald Smith phenomenon." Rosenau and Anderson showed that the first dose of serum has so changed the living chemistry of the organism as to make it more sensitive to the second. The latent period, or "incubation" time between the first and second dose, must elapse before this anaphylactic state is present. It is synchronous with the same period of von Pirquet's disease, five to thirteen days.

In the anaphylactic disease that I describe later for the first time, the incubation period varies from one to several days. All of the erythematous and urticarial skin eruptions due to shell fish, mussels, fruits, tomatoes, and other food proteins, have a relatively short incubation period. Although, in hypersensitized guinea-pigs, all of the serum proteins produce the characteristic signs by intravenous, hypodermic, intracerebral, or intraperitoneal doses, it is evident that in man alimentary or olfactory absorptions may also bring about a state of anaphylaxis. Hay fever and eruptive rashes are striking proofs of this. Within five minutes of inhaling the pollen proteins, or enjoying tomato proteins, the individual shows the particular anaphylactic reaction.

When the guinea-pig receives its dose, as a rule, ten minutes is a long time to wait for excitement and cries of discomfort from the little animal. Dyspnoea, respiratory distress. Cheyne-Stokes, or irregular respiration, gasping for breath, all soon give way to a paralytic stage. Convulsive tremors and spasms, with a fall of blood pressure usher in the animal's death. The heart and pulse may beat fifteen or thirty minutes after breathing has ceased.

Auer and Lewis' observations, confirmed by Anderson, Biedl, and Kraus, go to prove that this respiratory failure is not central, but peripheral in origin. They incline to the view that no air can enter or escape from the alveoli, because the bronchi are contracted and constricted. It is due to some chemical stimulation within the muscle bundles; for a previous injection of atropine will prevent this respiratory shock.

The incubation period in typhoid, tuberculosis, smallpox, malaria,

yellow fever, measles, and scarlatina is analagous in every way to the time that must elapse between a first and second dose of the protein, before the sensitizing reaction is possible. The earliest time may be four days, the longest three years. The second dose injected after twelve days, as a rule, shows the most pronounced phenomena.

Though the first dose of protein may be given by the intra-inoculatory route, the anaphylactic reaction may at the end of twelve days be produced by giving the same protein by the mouth. McClintock and King, however, proved this to be a less severe reaction than if given by any of the other syringe routes.

These varieties of reduced and accelerated responses, are discussed fully by von Pirquet. Vaccination does not produce a condition of prophylaxis, but hastens the action, and alters the potential into kinetic tissue reaction. This causes a reinfected individual to have a conclusive and rapid recovery. This is the allergie of von Pirquet: It is prophylaxis caused by the change of potential power into kinetic reaction.

When no clinical signs are manifested at the introduction of a foreign protein (endotoxins, living organisms, foods), there is a condition of active immunity and absence of susceptibility. Natural immunity may be a variety of active immunity, due to alexines, or adaptation. Passive immunity is obtained by the introduction of antitoxins or antibodies already made in another animal by active immunity.

If serum, egg albumin, or other protein be thoroughly dried, they may with impunity be heated for ten minutes to 170° C. or for two hours at 130° C. If this is then put into solution of 9 per cent. normal salt, it will be just as potent in its anaphylactic powers as the fresh protein. The sensitizing and poisonous principle is evidently one and the same, as Rosenau and Anderson have held for years. It is unaffected by precipitation dialysis, filtration under pressure, freezing, digestion by ferment, or exposure to the x -rays. The common inorganic salts do not alter it. The sensitizing principle may act as a ferment, for one one-millionth of a cubic centimeter of horse protein, and one twenty-millionth of egg albumin are sufficient to place a guinea-pig in the sensitized state; $\frac{1}{100}$ c.c. of the former is then enough to cause fatal anaphylactic shock. Gay and Southard transferred to a healthy, untreated animal, something that rendered it sensitive to a later inoculation of the protein. They claimed this to be a substance which is not absorbed by guinea-pig tissues, but is eliminated gradually and slowly. They named it "anaphylactin."

Otto, in Ehrlich's laboratory, showed that a sensitizing principle could be made apparent within twenty-four hours. This is done by inoculating untreated animals, with serum from sensitized ones. This he says, is due to depressing parts of the antigens.

Anderson holds that Otto's sensitizing principle should be called by a modification of von Pirquet's *allergie*, namely, *allergin*; on account of the power to produce an altered reaction of the organism. The Anderson-Otto *allergin*, acts in twenty-four hours, the Gay-Southard *anaphylactin*, in fifteen days.

The close relation of prophylaxis to anaphylaxis is well demonstrated simultaneously with the specificity of the sensitizing principle. When the proteins (endotoxins) of typhoid bacilli are extracted from the cells and inoculated into guinea-pigs, a second injection of the same typhoid protein twelve days later, bring about the same anaphylactic phenomena. A guinea-pig may be simultaneously sensitized to two, three, four, or more proteids. The animal's tissues differentiate each anaphylactic protein, just as it would several separate infectious diseases. Chemical changes indicate that the sensitizing principle is a specific and, perhaps, a chemical substance. Richet calls this a toxicogenic, but in itself a non-toxic, principle.

Allergin (the passive anaphylaxis of Otto and Anderson) appears about the tenth day. It is also present in animals that have been made strongly prophylactic, that is, raised to a high degree of immunity. In a word, these animals are insensible to the sensitizing substance. A neutral substance protects the cells from the circulating *allergin*. In 1906, McClintock and King first noticed a mild sensitizing power of proteins fed by the mouth. Anderson, in 1910, emphasized the fact that animals fed with foreign proteins are as strongly sensitized as when the protein invades the system hypodermically.

My work on the urticarial and erythematous food rashes has confirmed, clinically, Anderson's laboratory observations. Anaphylactin, allergin, or the other sensitizing principles, though transmitted by the mother, is not present in her breast milk, or in the father's spermatozoon. Susceptibility to tuberculin is present in the offspring of a tuberculous mother. Since the sensitizing principle of anaphylaxis is transmitted from the female guinea-pig to her young, its presence is easily demonstrated.

Anderson called attention to the fact that serious collapse or acute lethal effects in man are dependent less upon the toxicity of the serum, intervals of injection, and quantity of serum than upon natural or hereditary susceptibility of the affected person.

Hay fever sufferers, asthmatics, with the bronchial type of disease, and others who have horse or stable symptoms, are subject to virulent disturbances when antisera are given them, not because of the serum or the dosage, but because of their native sensitiveness.

As I mentioned above, the conclusions to be drawn from the aggregate studies go far to show that the sensitizing and toxic molecules of the invading protein are closely identical. Though the collected investigations and much valuable work inclines one to

this view, in the light of Ehrlich's helpful side-chain hypothesis, I cannot believe this to be the truth.

Inorganic salts, alkaloids, ferments, and physical measures have been used to free horse serum from the toxic molecules, but the latter remains unaffected. Serum heated to 100° C. for an hour seems to be free of the toxic molecules, though it sensitizes on the first inoculation. This does not prove that the toxic principle is independent of the sensitizing molecule. For large amounts of deteriorated (heated) serums are always required to produce toxic symptoms, and very minute amounts only to sensitize.

Wilfred H. Manwaring, of the Lister Institute of Preventive Medicine, in London, announced in September, 1910, the first ambitious study of the physiology of anaphylaxis. He made plethysmographic blood and respiratory pressure studies. Electrical reactions; therapeutic applications, and the results of nerve sectioning were all investigated with relation to a deep-seated primary manifestation. In his search for the anaphylactic molecule, he hit, as he calls it, upon "the discovery" that anaphylaxis is an explosive auto-intoxication of intestinal and hepatic origin. This auto-intoxication is inhibited, modified, or overcome by a more or less efficient anti-anaphylactic mechanism situated in part in other organs.

Anaphylactic animals (of many species) which recover from the shock of a serum injection, are for a time immune (insusceptible) to a second dose. Nevertheless, if one transfers the serum from these immune animals to normal ones of the same species, anaphylactic shock may be immediately observed. Then in turn, the latter will be immune (insensitive). This holds true even though the vessels and waste matters have been well washed. The tissues seem to yield a cellular product that is anti-anaphylactic.

If ligatures are tied about the vena cava and aorta above the diaphragm the upper part of the anaphylactized animal will not respond to an invasion of serum. This excludes all viscera above the diaphragm as involved in forming anaphylactin (allergen). The nervous system, bony and tissue, muscular and lymphatic systems, the heart, vessels, and lungs, are all innocent of involvement. If the ligatures are removed, an explosive shock may at once be manifest. We may eliminate by excision all of the abdominal organs, except the liver, without preventing anaphylaxis. To prevent the surgical shock of liver amputation, the portal circulation may be closed by cutting the intestines out, and then injecting leech extract. If now a canula is placed in the abdominal vena cava and the jugular, the liver is as good as amputated for circulatory purposes. That the liver is not the only viscus concerned in the physiology of anaphylaxis, is very probable.

Manwaring advances no certain proofs of the nature of his auto-intoxication. It may be due to split or conjugation portions of

the invading protein, of free hepatic or intestinal ferments, of the native internal secretions of those organs, or itself a specific internal secretion. Anaphylactin is possibly translatable into the functional powers of fixed visceral cells. Perceptions, amboceptors, complementary bodies, antitoxic bodies, and immune bodies generally, also have a similar complex relation to fixed tissue cells.

We are at present utilizing the physiological changes that occur after an injection of mixed strains of typhoid bacilli proteins. The phenomenon induced by a second injection is followed later by a high degree of immunity to typhoid. The practical significance of this for the prevention of typhoid, as I mentioned once before in this paper, is now recognized by the English, Japanese, and American War Departments. In Baltimore, Dr. William Royal Stokes has already vaccinated a number of local physicians with two doses of 300,000,000 typhoid bacilli, killed with 0.01 per cent. phenol solutions.

From the foregoing facts, it is but a step to the conclusion that the placental animal may occasionally invade the pregnant animal in such a way that the minor obstetrical toxemias, or even eclampsia may result. That such proteins have their origin in the placenta rather than the foetus is easily demonstrated. Some of the many examples to prove this are postpartum eclampsia and the impossibility of sensitizing a mother to the blood or other proteins of her offspring. Yet the mother animal may be made anaphylactic to the autolytic proteids of her own placenta.

That we may, in the light of the recent work before us, conclude that eclampsia and the mild as well as malignant toxemias of pregnancy are phenomena of anaphylaxis, I think, is the most promising clinical view to take. Investigations at the bedside and in the laboratory, will soon, and I trust for all time, decide this important matter.

At present, researches are in progress to prove that explosive types of epilepsy, pernicious anemias, scurvy, purpuric diseases, and various obscure metabolic maladies, are but manifestations of the individual against a particular protein.

I believe that this was absolutely proved in the cases reported by me of such food proteins as tomatoes, berries, crabs, and the like. The recognition of the offending protein, whether its invasion is per os or by injection, whether it is via the olfactory route or by way of the circulation direct, is of such clinical importance, that internists dare not longer ignore the applications of our present knowledge of anaphylaxis.

There is another example of the clinical application of this anaphylactic reaction which I must mention before concluding this paper. It has never been recognized before, but I feel at liberty to describe it prematurely in this place. In all of the dermato-

logical clinics of sea-coast or river towns, is seen in the crabbing season, an erythematous, progressive cellulitis of the hands, due to abrasions from the shells of crabs, lobsters, and other shell fish. Hundreds of persons are scratched, injured, and "bitten" by crabs, yet only about one-tenth of 1 per cent. of those bitten show this erysipeloid eruption. It spreads from the point of the finger or hand scratched, steadily just like its more dangerous analogue, erysipelas.

Dr. T. Caspar Gelehrst studied a number of these cases bacteriologically and found them sterile. There was no associated micro-organism. "Crab hand" has been a mystery, as far as its immediate etiology was concerned.

When we realize that such a small number of those exposed to this shell reaction really exhibit it, and when all of the other factors associated are taken into consideration, I believe you will agree with me, that the condition fits in exactly with what we should expect from individuals sensitive to shell proteins.

THE VACCINE TREATMENT OF PYORRHŒA ALVEOLARIS.

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PYORRHŒA alveolaris, or Rigg's disease, is one of the diseases that have been characterized as "the most common disease in the world." It is a condition that physicians have been prone to overlook or disregard. The recent revival of mastication, however, has recalled it to our attention. Dentists, on the other hand, have long been awake to its importance, because of its effect on the teeth and because they are called upon to treat it.

Its pathogenesis has called forth much earnest discussion among the dentists, and they are rather sharply divided into two camps. Those of one camp maintain that the determining factor in its etiology is some such constitutional trait as gout or the "uric acid diathesis." Those of the other party believe that pyorrhœa is essentially a local disease. Bacteria are constantly present in large numbers and great variety. It could scarcely be otherwise in a suppurative process in the mouth. There are, however, certain organisms which seem to predominate. In some cases this is the pneumococcus, in others streptococcus pyogenes, or micrococcus catarrhalis, or the pyogenic staphylococci; or these bacteria may be associated in various groupings.

The lesion has been studied in man and other mammals also, for it is by no means confined to the human species. It is fairly

common in dogs and other domestic animals and is seen in animals in the wild state. The process begins as an inflammation of the gum at its free border. It extends with varying rapidity to the structures along the roots of the teeth. The bony alveolar process is absorbed, the gum retracts, and the root of the tooth is laid bare. The tooth, thus deprived of its bony support, becomes loose and ultimately may fall out. In this manner teeth that are perfectly sound and free from caries are lost. Deep in the pockets calcium salts are deposited on the root of the tooth as a scale that can be scraped off only with great difficulty. Its presence seems to prevent healing of the suppurative process. Pus is discharged uninterruptedly into the mouth. Abscesses at the root of the teeth, called calcic abscesses, are common. The disease runs a very chronic course. It is usually noticed in the fourth or fifth decade and lasts for years, often until all the teeth are lost.

The symptoms are many—the discharge of pus, the looseness of the teeth, and pain which may be excited by contact with heat or cold or by the act of chewing. Sometimes the pain is nearly constant and it may be referred to other branches of the fifth nerve as a trifacial neuralgia. Mastication is seriously interfered with and the patient pays the penalty of this omission with various disturbances of digestion and nutrition. The pus which constantly flows into the mouth is very foul and the breath has a far reaching odor of putrefaction. The pus is swallowed and presumably poisonous substances contained in it are absorbed and impair the patient's health, causing anemia, chronic arthritis and other ailments. It must, however, be admitted that some sufferers from pyorrhœa possess robust health.

The dental treatment of this disease consists of thorough cleaning of the mouth in general and more particularly in scraping the calculus from the roots of the teeth with great care and patience on the part of the dentist and more or less severe pain on the patient's part. If this is done thoroughly many of the patients seem to recover, and the disease may not recur if unusual care in the toilet of the mouth is persevered in. In other patients, in spite of every precaution, the pyorrhœa is merely mitigated or returns after a few weeks or months. Although this dental treatment is often very efficient it is by no means ideal. A supplementary treatment that will check the destructive process more quickly and completely is a great desideratum.

A chronic, sharply localized inflammation, such as pyorrhœa is, seems peculiarly suited to treatment with bacterial vaccines. The earliest report of vaccine treatment of this disease that I have found is in the Erasmus Wilson Lecture, before the Royal College of Surgeons of England, in 1907 by Goadby.¹ Two years later,

¹ *Lancet*, 1907, i, 663.

he published a second report.² The result of treatment in his cases was very satisfactory. Not only was the pyorrhœa cured or greatly improved, but there was a striking relief from such associated ailments as dyspepsia, anemia, joint pains, and malaise. Beebe,³ of Boston, has reported seventeen cases treated with vaccines, with very good results. Eyre and Payne,⁴ of London, also reported quite successful results in the treatment of thirty-three cases of unusual severity. All of these physicians made cultures from the infected gums, isolated and identified the more prominent organisms, and determined the patient's opsonic index to the various bacteria isolated from his mouth. Autogenous vaccines for every case containing one or more of the organisms to which the opsonic index pointed as causative were then prepared.

My interest in this treatment was stimulated by my friend, Dr. Arthur H. Merritt, a dentist, who has given much thought to pyorrhœa and who felt that some cases needed something more than even the most careful dental treatment.

The difficulty attending opsonic determinations is so great that I decided to venture upon the vaccine treatment without their help. The vaccines were obtained in the following manner: The gum and tooth were cleaned with a cotton swab and sterile water. A platinum loop was then inserted into the recess under the gum and along the root of the tooth. Pus obtained in this way was smeared on a slide and also used to inoculate Petri plates containing nutrient agar. After twenty-four hours of incubation at 37° C. the plates were sent to Dr. Charles Krumwiede, who prepared the vaccine from the organisms that seemed to predominate on the plate. After the vaccine had been standardized and its sterility established, it was sent to me for use. The sites chosen for injection were the interscapular and subscapular regions of the back and the deltoid region. The skin was cleaned with alcohol. Sometimes on the day or two after the injection, the discomfort in the teeth was somewhat aggravated, but this was regularly succeeded by decided improvement. Probably determinations of the opsonic index would have shown that this transitory exacerbation was the expression of the negative phase. The severest symptom of this sort that I saw was acute swelling of a lymph node in the floor of the mouth. After a few days this resolved perfectly, although at first it looked very threatening. In two other patients an abscess formed at the root of one of the teeth during treatment. Inasmuch as such abscesses were of frequent occurrence in both patients it is doubtful whether the vaccine was responsible.

The cases that I have treated fall into two groups. The first group includes eight cases who received autogenous vaccines.

² *Lancet*, 1909, ii, 1875.

³ *Boston Med. and Surg. Jour.*, 1909, clxi, 613.

⁴ *Proceedings Royal Soc. Medicine, Odontological Section*, 1909, iii.

These were all intractable cases of long standing and had been carefully treated by dentists. This should be remembered in judging of the value of the treatment. The second group embraces about a dozen dispensary patients in whom the effect of stock vaccine was tried. The cases of the first group are reported in detail in the following notes:

. CASE I.—A woman, aged about thirty-five years, a sufferer from pyorrhœa for ten years. Five teeth had been extracted. All of the remaining teeth were affected. They were loose, very sensitive to heat and cold and to mechanical shock. Pus exuded from all of the sockets. For four years careful dental treatment had been given at intervals. After every course of treatment the condition improved greatly, and except for persistent sensitiveness to heat and cold, the patient was comfortable for a while. After a time, however, the pyorrhœa recurred. During the year preceding the administration of vaccines, the relief from dental treatment was less complete and the intervals of comparative comfort grew progressively shorter, until the remission lasted for a few weeks only. This patient was referred to me by Dr. Merritt. The dominant organism in the culture was a streptococcus and the vaccine was made from this. The patient received eleven injections within a period of thirteen weeks. The respective doses in the order of their administration were 10,000,000, 16,000,000, 24,000,000, 36,000,000, 30,000,000, 30,000,000, 34,000,000, 30,000,000, 30,000,000, 90,000,000, and 80,000,000 of killed bacteria. After the third dose, the patient said that she was as comfortable as after any course of dental treatment. Some pus, however, was still present. In the following week Dr. Merritt resumed the local treatment. Some of the doses of vaccine were followed for a day or two by increased sensitiveness of the teeth, probably an expression of the negative phase. The intensity and duration of these symptoms served to determine the size of the next dose. For example, after the fourth dose, the negative phase was obvious for two days and consequently the fifth dose was reduced. The dose of 90,000,000 was unintentionally large, but by this time the patient's immunity seemed to have reached a high level; at any rate, she felt better after it. The treatment resulted in a cure of the pyorrhœa—by this, I mean, that the patient felt perfectly comfortable even while chewing or while drinking hot or cold liquids, there was no formation of pus, no pockets around the teeth, and the gums looked healthy. Twenty months after the cessation of all treatment the pyorrhœa had not recurred.

CASE II.—A woman, aged about thirty-seven years. Pyorrhœa for five years. For two years she received active local treatment from Dr. Merritt by which she was greatly benefited, but she was not cured. After a two years' absence from the city she again consulted Dr. Merritt, who found that the pyorrhœa

had advanced considerably. Most of the teeth were loose, there was a free discharge of pus, much absorption of the bony alveolar process, great sensitiveness to heat and cold, and chewing was very painful. Several calcic abscesses had formed during her absence from the city. Without giving her any local treatment, whatever, Dr. Merritt sent her to me. Streptococci predominated in the culture. While waiting for the autogenous vaccine, she received at weekly intervals three doses of a streptococcus vaccine from another case of pyorrhœa. The doses were 20,000,000, 30,000,000, and 40,000,000. After these injections her teeth were more comfortable than at any time for years, but some sensitiveness to cold persisted. The objective improvement was less striking. There was still a discharge of pus from the pockets around the teeth. At this time Dr. Merritt began local treatment and, also, the use of her autogenous vaccine was commenced. The doses in order were of 25,000,000, 35,000,000, 50,000,000, 65,000,000, 75,000,000, 80,000,000, and 75,000,000. The interval between the doses was in every instance one week. At the conclusion of the treatment she was apparently cured. Eighteen months later there was no evidence of a recurrence.

CASE III.—A woman, aged forty years. Thirty teeth were affected. She presented a most severe case. Interference with her general health was shown by a loss of vigor and energy. Instead of leading a very active life she had become languid and felt unequal to any exertion. This patient also was sent me by Dr. Merritt. An autogenous vaccine was made from streptococci found in the cultures from her gums. In addition to rapid improvement in the condition of her mouth, her former vigorous health returned after a few injections and she resumed her former activities with enthusiasm. She received fourteen injections in a period of fifteen weeks. Two months after the last dose, Dr. Merritt found a single pocket discharging pus. Elsewhere her pyorrhœa seemed cured. The treatment of this case was too recent to allow any further statement as to the permanency of the improvement.

CASE IV.—A man, aged fifty years. A severe case sent by Dr. Merritt. The autogenous vaccine contained streptococci and staphylococci in the ratio of 1 to 2. Within a period of seven and a half weeks nine injections were given, the dose ranging from 6,000,000 to 60,000,000 of streptococci with twice the number of staphylococci. This case, also, was apparently cured. Three months later there was no recurrence.

CASE V.—A man, aged fifty-five years. Pyorrhœa for many years. He had already lost several teeth and had been told by his dentist that several others were so loose that they, too, would certainly fall out. This was a very severe case. During a period of thirty weeks he received eighteen injections of an autogenous streptococcus vaccine, the dose increasing from 10,000,000 to 50,000,000. The

improvement in the pyorrhoea was very striking and all subjective symptoms disappeared. Although expressing great delight with his increased comfort, this patient would not come regularly for treatment.

CASE VI.—A man, aged sixty years. General and obstinate pyorrhoea. He was sent to me by his dentist, Dr. Joseph M. Levy. At weekly intervals thirteen injections of an autogenous streptococcus vaccine were given. The dose was increased from 7,000,000 to 53,000,000. This treatment led to an apparent cure. Eight months after the last injection, his dentist reported that a slight amount of pus was found in the socket of a single tooth.

CASE VII.—A woman, aged forty-five years, sent by Dr. Levy. She, also, presented a very severe case. During the treatment some teeth with practically no bony support were extracted. She received eighteen injections of an autogenous streptococcus vaccine at weekly intervals. The dose ranged from 6,000,000 to 90,000,000. When a dose of 12,000,000 was reached, she exhibited symptoms of a negative phase. On the day following the injection, her teeth were slightly more painful, on the next day the pain was quite troublesome, but after this the teeth felt distinctly more comfortable than before the injection. This patient, also, seemed to be cured.

CASE VIII.—A woman, aged about thirty years. Sent to me by Dr. Leavitt. For fifteen years she has had an abscess cavity at the root of one of the incisors that discharged pus intermittently. The gums elsewhere, although not healthy were much less severely affected. While waiting for her autogenous vaccine, she received two injections of a mixed streptococcus vaccine from cases of pyorrhoea in doses of 12,000,000 and 16,000,000, respectively. Later, she received two injections of autogenous streptococcus vaccine. She then left the city for the summer. Although the treatment in this case was very brief, its good effects seemed to show in an unwonted decrease in the discharge of pus and in a much healthier condition of the gums in general. This improvement persisted for at least three months, the time of the latest report. The treatment with vaccine will be resumed upon her return to the city.

In addition to these cases treated exclusively or chiefly with autogenous vaccine, I have tried stock vaccine in thirteen cases in the dental clinic of Dr. Henry S. Dunning. Of these patients, four did not return after the first injection. Two others disappeared after the second dose. Of the rest, two received three injections each, and in one of these the discharge of pus was much reduced. One patient got four injections at weekly intervals. When she returned for the fourth dose the discharge of pus, which had been very profuse, was scarcely discernible. She did not return again until a month later and then the pus was almost as abundant as at first. Of the remaining patients in this group, three received seven injections each. Two of these were greatly improved in both subjective

and objective symptoms. They were perfectly comfortable and their gums looked normal except for the retraction along the roots of the teeth due to destruction of bone. The third patient showed only a moderate improvement. Perhaps she needed a different vaccine. Finally one patient received nine doses, increasing from 12,000,000 to 120,000,000. She seemed to be cured. All of these patients had suffered for a long time, and in most of them the pyorrhœa was very severe. On the whole, the results with the stock vaccine were encouraging. The vaccine was made by mixing together in equal proportions four of the vaccines made for the treatment of cases reported in this paper. None of the cases in this group from Dr. Dunning's dispensary received any dental treatment whatever, further than advice about the use of the tooth brush. It is too much to expect patients to recover fully until the calcareous deposits on the roots are carefully removed by a dentist. I dare not as yet formulate an opinion as to the limitations and possibilities of stock vaccines. In some cases they were undoubtedly very satisfactory, but whether they can lead to such long remissions as may follow the autogenous vaccines I do not know.

At times in trying to decide upon the dosage of the vaccines I have felt that a knowledge of the patient's opsonic index would have given me more confidence. By proceeding carefully, however, no harmful results were encountered. The patients treated with autogenous vaccines were so greatly benefited that it seems reasonable to attempt this treatment, relying only on the patient's symptoms and the physician's experience to control the size of the dose.

It was most satisfactory to note the general improvement in health of many of the patients. Doubtless this was due, in part, to their release from pain and discomfort of the teeth, and in so far was due to psychological causes. In part, it was due to their ability to eat more food and to chew it properly. Although recognizing the influence of these factors, one cannot escape the conviction that the elimination of the sepsis from the suppuration around the teeth was of importance in the restoration of health.

Of course, the partial exposure of the roots of the teeth due to absorption of the bone cannot be repaired, but we may hope that the vaccines together with careful dental treatment may stop the advance of the disease and enable the patient to keep with comfort such teeth as still have a reasonable bony support.

THE RESULTS OF MEDICINAL TREATMENT IN ELEVEN HUNDRED AND SIX CASES OF DELIRIUM TREMENS.

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NOTWITHSTANDING the considerable discussion which the subject has received, the treatment of delirium tremens is very unsatisfactory; and there is little agreement among the various writers as to the best method of procedure. Some advise hypnotics in large doses, others regard them as dangerous in even the smallest quantities, believing that they never shorten the delirium and often unfavorably influence an already weakened heart. Whether whisky should be used is a mooted question, as is also the use of digitalis and other stimulants. Sedative baths are recommended by some and condemned by others. In view of these facts there seems to be sufficient justification for a further study of the subject.

COLLECTION OF THE STATISTICS. Of the 1106 cases on which this paper is based, 934 were under treatment in the Cook County Hospital, Chicago, during the years 1905 to 1910 inclusive. The 172 remaining cases were treated at the Massachusetts General Hospital. It was thought best, for reasons soon to be given, not to include the latter in the detailed analysis to which the Cook County Hospital cases were subjected, and they are considered separately throughout this paper. Five hundred of the Cook County Hospital cases, treated from 1905 to 1908, were made the basis of an earlier report;¹ the remaining 434 were collected at a later date.

In collecting the statistics the original history was examined in each case and the relevant facts transcribed on a library card. Each card was made to show the age and sex of the patient, whether the case was incipient or fully developed, whether it developed from the first to the second stage in the hospital, and if so, after how long and under what treatment, and also to show each drug used, with the size and number of the doses, together with the results of the treatment and the complications. The cards could then be readily sorted and the cases classified according to any one of the points noted. A considerable number of these cases, though by no means the greater part, have been under the observation of one or the other of us. For permission to examine the hospital records, our thanks are due to the authorities in charge of the Cook County Hospital and of the Massachusetts General Hospital.

COURSE OF THE DISEASE. The course of the disease presents two quite sharply defined stages: an incipient stage characterized

¹ Jour. Amer. Med. Assoc., 1909, p. 1224.

by insomnia, restlessness, tremor, and occasionally by hallucinations, which are, however, recognized as such, and later a stage of delirium characterized by uncorrected, chiefly visual hallucinations. The patients in the second stage are usually fearful but may be amused by their visions and are very noisy, with great incoördination. There is usually fever, 100° to 102° F., slight leukocytosis, 7000 to 9000, and profuse perspiration. Since these two phases of the disease are as sharply defined in their reaction to medicinal treatment as they are in their clinical manifestations, and since many of the incipient cases never become delirious, it is of fundamental importance that statistics should take this distinction into consideration. But this distinction has not been recognized as having any significance in connection with treatment. Only in the preliminary report² published by one of us in 1909, and in a paper by Porter³ which has since appeared, has there been any account taken of these two stages in compiling the statistics.

Throughout this report the two stages are considered separately, and for brevity will be spoken of as first and second stages respectively. Since some cases develop from the first to the second stage in the ward they have entered twice into the tables given below. Among those from the Cook County Hospital there were 430 of the first stage that never became delirious and 272 that did, making the total number of first stage cases 702. On the other hand, there were 233 cases admitted to the hospital in the second stage, and these with the 272 that became delirious in the wards make a total of 505 for the second stage. Thus, due to the fact that 272 cases are each represented twice in the tables, there appear to be a total of 1206 instead of 934 for both stages.

COMPLICATIONS. In the series of five hundred cases, previously reported, very few with serious complications were included, for in collecting these histories only the files on alcoholism were consulted. Of fractures there were 13 and of pneumonia 14 instances. In the second series the files on fractures were also examined, and 61 with delirium tremens were secured. The extent to which other complications entered into this second series is indicated in Table I. Altogether there were 88 complicated cases and they have been entered separately in the tables given below.

TABLE I.—Complications in the Second Series.

Fractures	61
Pneumonia	8
Nephritis	5
Pulmonary œdema	1
Infection of hand	1
Burn of hand	1
Ulcers	8
Contusion of hip	1
Psoriasis	1
Dislocation of clavicle	1

² Jour. Amer. Med. Assoc., 1909, p. 1224. ³ Die Therapie der Gegenwart, 1910, p. 270

MORTALITY. We have given in Table II a tabulation of the mortality in delirium tremens as reported by various writers. The hospitals in which the cases were treated and the number of cases on which the percentages were based are given wherever these facts could be readily obtained. It will be seen that the mortality has varied greatly, Boston reporting a mortality of 37 per cent. and Moller 2 per cent. Now it is obvious to any one who reads these reports that this difference is not due entirely or even for the greater part to the treatment used. A much more important factor is found in the variation of the type of cases received at the various hospitals. Such a variation might be due to a difference in the alcoholic drinks taken in different countries. One cannot read the German and Scandinavian accounts without being impressed with the fact that their cases are much more responsive to treatment than are those in our own hospitals. It is also probable that in different hospitals there is a wide difference as to the line drawn between chronic alcoholism and incipient delirium tremens. Furthermore, in some hospitals much more adequate nursing can be given than in others. Porter has recently called attention to this fact, stating that from a comparison of the mortality in different clinics it was not possible to draw any conclusion as to the value of the varying methods of treating these patients, for the reasons which we have already stated. But, he adds, where the same criteria can be applied to a homogeneous group of cases treated in a single hospital, valid conclusions may be drawn as to the efficacy of different methods of treatment employed. So far as we know, statistics of this sort have been published only by Ganzer, Porter, and ourselves.

TABLE II.—Mortality in Delirium Tremens.

			Per cent.
Moller ⁴	100	2	2.0
Krukenberg ⁵	161	16	10.0
Franque (after Krukenberg)	2117	387	18.0
Näcke (after Krukenberg)	24.3
Weiss (after Krukenberg)	13.8
Eichelberg ⁶	1574	..	5.5
Boston ⁷	140	52	37.0
Ganser ⁸	1051	36	3.4
Kraepelin (after Eichelberg)	15 to 20.0
Jacobsen (after Eichelberg)	19.0
Krafft-Ebing (after Eichelberg)	15.0
Bonhöffer (after Eichelberg)	9.0
Calmeil (after Eichelberg)	5.6
E. von der Porter ⁹	660	45	6.8

⁴ Frederiksberg Hospital, Copenhagen.

⁵ Allg. Krankenhaus, Hamburg Eppendorf.

⁶ Ibid.

⁷ Philadelphia Hospital (Blockley).

⁸ Stadtischen Heil und Pflegeanstalt zu Dresden.

⁹ Allg. Krankenhaus, St. George, Hamburg.

TABLE III.—Mortality in Delirium Tremens.

COOK COUNTY HOSPITAL.			Mortality
Group	Cases	Died	Per cent.
All cases, 1905 to 1910	934	206	22.0
All cases, 1905 to 1908	500	132	26.4
All cases, 1908 to 1910	434	74	17.0
All first stage cases	702	8	1.1
All second stage cases	505	198	39.2
Uncomplicated second stage cases, 1908 to 1910 . .	147	40	27.2
Complicated second stage cases, 1908 to 1910 . .	57	26	45.6

MASSACHUSETTS GENERAL HOSPITAL.			
Entire series	172	102	59.3
Uncomplicated	60	21	35.0
Complicated	112	81	72.3

Among the Cook County Hospital cases 206 out of 934 died, or 22 per cent., and of these, 198 were among the delirious patients, only 8 out of the 702 incipient cases terminating fatally, and in these 8 the lethal termination was obviously due to associated conditions, especially in the heart and lungs. Also note that during the first two and one-half years the mortality was 26.4 per cent., dropping to 17 per cent. during the second two and one-half years. Reasons for this decrease will be given later.

The mortality of 22 per cent. for the entire series (Cook County Hospital) corresponds with that reported by Franque, Näcke, Kraeplin, Jacobsen, and Krafft-Ebing, but is considerably higher than that given by other writers. It must be borne in mind, however, that these are American patients and there is some evidence to show that the mortality from delirium tremens is higher here than in Europe. The series of cases reported by Boston from the Philadelphia Hospital gave a mortality of 37 per cent. and the mortality in the Massachusetts General Hospital is even higher.

The mortality in the Massachusetts General Hospital, however, requires a word of explanation. It was obvious on examining these histories that the diagnosis of delirium tremens had been restricted to second stage cases, only a very few incipient cases having been diagnosticated and classified under that head. A very large percentage of the cases were complicated and this fact also increases the mortality. In order to compare the mortality in the two hospitals, the second stage cases in the Cook County Hospital from 1908 to 1910 have been divided into a complicated and uncomplicated group, and the death-rate computed separately. When these are compared with the complicated and uncomplicated cases in the Massachusetts General Hospital it is seen that the mortality in the latter is somewhat higher. These facts emphasize the statement already made that it is unsafe to compare the gross mortality from delirium tremens in two hospitals, and from the comparison draw conclusions concerning the treatment of delirium tremens.

TREATMENT. In this paper we will limit ourselves to a discussion of the results obtained by the administration of drugs; but in order to render possible the comparison of our results with those of others it is necessary to give in brief the usual method of nursing employed in delirium tremens in the Cook County Hospital. The patients are usually allowed to walk about the ward in the incipient stage unless confined to bed by some other malady. They are put in bed as soon as they become delirious and are retained there by mechanical means. Elimination is maintained by the administration of a cathartic on entrance and a free use of water and liquid foods. Hot baths and packs are seldom given. Variations from this manner of handling the cases are not taken into account because they will average themselves out in a long series.

Usually more than one drug is used in an individual case, and it has not been possible to compare a series of cases in which one was used alone with another series in which a different one was used by itself. In order to determine the value of any drug the cases were divided into two groups according to whether or not it was employed. All other factors will be the same in the two groups. For example, some patients receiving veronal will also be given whisky and others will not; and of those not receiving veronal whisky will be given to some and not to others. Such additional drugs will thus act as any other variables and average themselves out of the result in a long series. This would not be the case if any two drugs were habitually used in combination—but the only approach to this is the somewhat common combination of whisky and ergot. In order to determine how commonly such a combination occurred, all of the complicated cases in the second series were examined and it was found that there were 20 on ergot, 11 on ergot and whisky, and 12 on whisky, which shows that even these drugs were more commonly used separately than together.

Hypnotics. There is no uniformity of opinion as to whether hypnotics have any influence in cutting short an attack of delirium tremens. The enormous doses usually employed are often without effect, or if a short sleep is produced the patient awakens from it with unabated delirium. When the disease has run its course the patient falls into a profound sleep from which he awakens more or less himself. That this critical sleep can be induced by hypnotics is very doubtful and those usually used have proved so dangerous that in many quarters the use of all these drugs has been entirely eliminated. Rolleston,¹⁰ Eichelberg,¹¹ Ganser,¹² Kerr,¹³ Legrain,¹⁴

¹⁰ System of Medicine (Allbutt and Rolleston).

¹¹ München. med. Wochenschr., 1907, p. 978.

¹² Ibid., p. 120.

¹³ Twentieth Century Practice (Stedman), 1895, vol. iii.

¹⁴ Presse Méd. Par. 1907, p. 790.

Bonhöffer,¹⁵ Kraeplin,¹⁶ and Petty¹⁷ either do not use them at all, or else employ them late in the course of the disease and in a very small quantity. Aufrecht¹⁸ and Harnack¹⁹ on the other hand recommend the use of large doses of sedatives, especially chloral, maintaining that the treatment is efficacious and free from danger. Others take an intermediate position.

It is noteworthy that these two authors have laid stress on the value of hypnotics in putting delirious patients to sleep, paying little or no attention to its efficacy in preventing the first stage of the disease being transformed into the second. Now, as will be shown later, it is on the incipient cases that these drugs act most effectively. To illustrate, the effect of the drugs on the two classes of cases we have divided the 934 cases into two groups, representing the first and second stages of the disease. It also seemed desirable to maintain separately the first series of 500 and the second series of 434, and to redivide this second group into complicated and uncomplicated cases. This will give the reader a chance to determine the distribution of the cases and the effect of any drug on any particular group.

TABLE IV.—Use of Chloral in the First Stage.

		Chloral used		Chloral not used	
		Total	Dev.	Total	Dev.
First series		85	18	260	127
Second series	Uncomplicated	24	8	260	70
	Complicated	3	2	70	47
		<hr/>	<hr/>	<hr/>	<hr/>
		112	28	590	244
Percentage becoming delirious		25%		41.3%	

TABLE V.—Use of Chloral in the Second Stage.

		Chloral used.		Chloral not used.	
		Total.	Died.	Total.	Died.
First series		145	65	156	67
Second series	Uncomplicated	31	5	116	35
	Complicated	7	5	50	21
		<hr/>	<hr/>	<hr/>	<hr/>
		183	75	322	123
Mortality		40.9%		38.2%	

Chloral is one of the most commonly used of these drugs and is given the preference by Aufrecht, Harnack, and Krukenberg,²⁰ while it is considered extremely dangerous by Eichelberg, Ganser, and Legrain. It was used somewhat less extensively than the bromides in the Cook County Hospital. The dose varied from 10 to 30 grams often repeated every four hours and frequently combined with some other sedative as bromide or morphine. It will

¹⁵ Cited by Moller.

¹⁶ Cited by Moller.

¹⁷ Alabama Med. Jour., 1909, p. 779.

¹⁸ München. med. Wochens., 1907, p. 1589.

¹⁹ Handbuch der Praktischen Medizin (Erbstein und Schwalbe), 1906, vol. iv.

²⁰ Zeitschrift f. klinische Medizin, vol. xix, sup. Hefte, p. 1.

be clear from a glance at the tables that it acts very differently in the first and second stages of the disease. While our data do not permit us to draw any conclusion as to its ability to induce the critical sleep, yet it is obvious that on the whole its effect on the delirious patients was unfavorable, the mortality in the 183 cases in which it was used being 2.7 per cent. higher than in the 322 cases in which it was not used. Its effect on the circulation more than counterbalanced any good it did. Quite a different result is noticed in incipient delirium tremens. Of the 112 such patients treated with chloral, only 25 per cent. became delirious, while of the 590 not so treated, 41.3 per cent. did develop delirium. It therefore possesses a marked influence in preventing the disease from passing from the first into the second stage.

TABLE VI.—Use of Bromides in First Stage.

		Bromides used.		Bromides not used.	
		Total.	Dev.	Total.	Dev.
First series		189	62	157	83
Second series	Uncomplicated	115	18	169	60
	Complicated	17	7	55	42
		321	87	381	185
Percentage developing delirium		27.1%		48.6%	

TABLE VII.—Use of Bromides in the Second Stage.

		Bromides used.		Bromides not used.	
		Total.	Died.	Total.	Died.
First series		198	90	103	42
Second series	Uncomplicated	68	19	79	21
	Complicated	24	10	33	16
		290	119	215	79
Mortality		41.0%		36.7%	

Bromides have been less discussed than chloral, being apparently considered both less dangerous and less effective. In the Cook County Hospital they were very extensively used in doses of 30 to 90 grains, repeated every four hours. The results given by the bromides were not very different from those obtained by the use of chloral. The delirious patients were certainly not benefited by their use, there being a mortality of 41 per cent. when they were used as against 36.7 per cent. when they were not used. Of the incipient cases, however, that received them, only 27.1 per cent. became delirious as against 48.6 per cent. among those that did not receive them.

TABLE VIII.—Use of Paraldehyde in the First Stage.

		Paraldehyde used.		Paraldehyde not used.	
		Total.	Dev.	Total.	Dev.
First series		28	5	256	73
Second series	Uncomplicated	4	1	69	48
	Complicated				
		32	6	325	121
Percentage becoming delirious		18.8%		37.3%	

TABLE IX.—Use of Paraldehyd in the Second Stage.

		Paraldehyd used.		Paraldehyd not used.	
		Total.	Died.	Total.	Died.
First series	
Second series	Uncomplicated	20	8	127	32
	Complicated	2	0	55	26
		22	8	182	58
Mortality		36.4%		31.8%	

Paraldehyde has not been extensively used and practically nothing is said concerning it in the literature on this subject. In the first series only a few cases were treated with it, but in the second there were a sufficient number to justify their tabulation. Its action seems to be very similar to that of chloral and the bromides, slightly increasing the mortality in the delirious patients and very considerably lessening the danger of an incipient case becoming delirious.

TABLE X.—Use of Morphine in the First Stage.

		Morphine used.		Morphine not used.	
		Total.	Dev.	Total.	Dev.
First series		70	27	275	118
Second series	Uncomplicated	82	25	202	53
	Complicated	12	7	61	42
		164	59	538	213
Percentage becoming delirious		35.9%		39.6%	

TABLE XI.—Use of Morphine in the Second Stage.

		Morphine used.		Morphine not used.	
		Total.	Died.	Total.	Died.
First series		150	64	151	68
Second series	Uncomplicated	84	33	63	7
	Complicated	37	18	20	8
		271	115	234	83
Mortality		42.4%		35.4%	

Morphine and opium were once very extensively used and Rolleston and Harnack still recommend them. They are, however, both useless and dangerous. We do not intend to go into the theoretical reasons against the use of morphine, believing that it is sufficiently condemned by its own results as given in the table. In the delirious patients it increased the mortality more than chloral, paraldehyde, or the bromides, and in the incipient cases it had little if any effect in warding off the stage of delirium. The dose of morphine was usually one-quarter of a grain, repeated at intervals of four hours.

TABLE XII.—Use of Hyoscine in the First Stage.

		Hyoscine used.		Hyoscine not used.	
		Total.	Dev.	Total.	Dev.
First series		39	15	306	130
Second series	Uncomplicated	21	3	263	75
	Complicated	2	2	71	47
		62	20	640	252
Percentage becoming delirious		32.2%		39.3%	

TABLE XIII.—Use of Hyoscine in the Second Stage.

		Hyoscine used.		Hyoscine not used.	
		Total.	Died.	Total.	Died.
First series		110	56	191	76
Second series {	Uncomplicated	31	14	116	26
	Complicated	9	6	48	20
		<hr/>	<hr/>	<hr/>	<hr/>
		150	76	355	122
Mortality		50.7%		34.3%	

Hyoscine. Legrain, who seldom uses a hypnotic in these cases, states that whenever one is imperatively demanded he prefers hyoscine to any of the others. But the drug has not been generally recommended. When given to these patients in the Cook County Hospital (dose $\frac{1}{100}$ to $\frac{1}{50}$ gr.) it proved itself to be very dangerous, the mortality in the delirious patients being increased by its use 16.4 per cent. It is of less service than chloral, paraldehyde, or the bromides in preventing the transformation of the first into the second stage.

We feel justified from these results in saying that neither morphine nor hyoscine should be used in the treatment of delirium tremens, but of the two hyoscine is undoubtedly the worse.

TABLE XIV.—Use of Veronal in the First Stage.

		Veronal used.		Veronal not used.	
		Total.	Dev.	Total.	Dev.
First series		85	9	199	69
Second series {	Uncomplicated	6	4	67	45
	Complicated	<hr/>	<hr/>	<hr/>	<hr/>
		91	13	266	114
Percentage becoming delirious		14.3%		42.8%	

TABLE XV.—Use of Veronal in the Second Stage.

		Veronal used.		Veronal not used.	
		Total.	Died.	Total.	Died.
First series		50	8	97	32
Second series {	Uncomplicated	16	6	41	20
	Complicated	<hr/>	<hr/>	<hr/>	<hr/>
		66	14	138	52
Mortality		21.2%		37.6%	

It will be noticed that the drugs so far mentioned have increased the mortality when given to delirious patients. The only hypnotic that did not have this effect was veronal. This drug was used but seldom in the first series and has therefore been tabulated only in the second. Of the 66 cases in the second stage receiving veronal, 14 died, or 21.2 per cent., while of the 138 not receiving it 52 died, or 37.6 per cent., making a decrease in the mortality of 16.4 per cent. It was also superior to the other hypnotics in its action on the incipient cases. Of 91 such treated with veronal 13 became delirious,

or 14.3 per cent., while of the 266 not so treated 114 became delirious, representing a decrease due to veronal of 28.5 per cent.

From our personal experience with these cases we can say that the superiority of veronal over the other hypnotics is quite as easily recognized at the bedside as from tabulations such as these. It is possible to produce a pronounced sedative effect on the nervous system without any disturbance of the circulation (Köhler), and all recorded cases of veronal poisoning are said by Porter to have shown that it does not depress the circulation. If the statements by Köhler and Porter are correct it is easy to understand why veronal is superior to the other hypnotics in the treatment of a disease where the heart is so often in a weakened condition.

Similar results have been obtained by others. Porter reports a series of 660 cases treated at the Allgemeine Krankenhaus, St. George, Hamburg, from 1901 to 1909. From 1901 to 1906, during which time there were 396 cases, chloral and bromides were used with 36 deaths, or 9 per cent. From 1906 to 1909 there were 264 cases almost exclusively treated with veronal with 9 deaths, or 3.4 per cent. At the same time the number of cases developing from the first to the second stage in the hospital was reduced from 18 per cent. to 5.6 per cent.

Moller²¹ also reports that until 1903 they had used an expectant plan of treatment for these cases in the Fredericksburg Hospital, Copenhagen, having previously found all hypnotics useless. Since 1903 they have used veronal with excellent results. But he does not compare the mortality before and after the use of veronal was begun. Friedreich²² has also reported on the use of veronal in delirium tremens, but his paper is not accessible.

It is clear that the hypnotics as a class act much more favorably on the incipient than on the fully developed cases, each having reduced the number passing from the first into the second stage. But morphine and hyoscine are much less effectual in this regard than the others. Since in some cases more than one hypnotic was used, the results cannot be taken as absolute. A drug like morphine, since it was sometimes used with chloral, may owe its apparent slight value to such an occasional combination with a more effective drug. To what extent such combinations occurred can be judged from Tables XVI and XVII.

TABLE XVI.—The Effect of Hypnotic Drugs in General on Incipient Delirium Tremens.

	Total.	Dev.	Per cent.
On any hypnotic	538	167	31.0
On no hypnotic	165	107	64.8

²¹ Berl. klin. Wochensh., 1909, p. 2340.

²² Urgeskrift for Laeger, December, 1909.

TABLE XVII.—The Effect of Individual Hypnotic Drugs on Incipient Delirium Tremens.

	Total.	Dev.	Per cent.
On morphine	164	59	35.9
On hyoscine	62	20	32.2
On bromide	321	87	27.1
On chloral	112	28	25.0
On paraldehyde	32	6	18.8
On veronal	91	13	14.3

Table XVI shows that it is possible in the majority of incipient cases to arrest the course of the disease by the use of hypnotics. Of the cases to which such drugs were administered only 31 per cent. became delirious as against 64.8 per cent. of those not so treated. This emphasizes the fact that it is of the utmost importance that the responsiveness of the incipient cases to treatment should be recognized, and the patient given the benefit of treatment at the onset of the first symptoms.

Table XVII presents the hypnotics arranged in order from the least to the most efficient. It will be seen that the sum of the numbers representing the totals in Table XVII is 782 or 244 more than the number of cases (538) that were given hypnotics. Hence almost one-half of the cases received two or more such drugs in combination. Of course a drug like morphine which has little if any value would profit in these statistics by an occasional combination with a more efficient drug, and, while the relative positions of the drugs in Table XVII are correct, there is actually more difference in their value than is there represented.

Alcohol. The use of alcohol is almost universally condemned at the present time. Lambert,²³ Aufrecht, Eichelberg, Kraeplin, Bonhoffer, Porter, Harnack, Kerr, and Legrain, who speak from experience in large hospitals in England, Germany, France, and America, say that it should be used if at all only in the cases complicated with some serious condition like pneumonia. Edwards²⁴ advises the continuation of alcohol in moderate doses.

So far as we have been able to ascertain the objections to alcohol by the above named authors are upon theoretical grounds. They say that, since it has been shown that the withdrawal of alcohol cannot of itself precipitate an attack of delirium tremens in a chronic alcoholic, it is not necessary that it should be given to patients presenting symptoms of incipient delirium tremens. And since delirium tremens is obviously a toxemia based upon chronic alcoholism, the alcohol should at once be withdrawn to lessen such toxemia. We have not encountered in the literature any evidence to show that the withdrawal of alcohol decreases the mortality from delirium tremens or decreases the number of cases developing

²³ System of Medicine (Osler).

²⁴ Practice of Medicine.

delirium. In the absenc of such evidence we feel that facts to be presented should outweigh theoretical considerations.

TABLE XVIII.—Use of Alcohol in the First Stage.

		Alcohol used.		Alcohol not used.	
		Total.	Dev.	Total.	Dev.
First series		110	31	235	114
Second series	Uncomplicated	80	14	204	64
	Complicated	12	4	61	45
		202	49	500	223
Percentage becoming delirious		24.3%		44.6%	

TABLE XIX.—Use of Alcohol in the Second Stage.

		Alcohol used.		Alcohol not used.	
		Total.	Died.	Total.	Died.
First series		131	59	170	73
Second series	Uncomplicated	69	16	78	24
	Complicated	17	8	40	18
		217	83	288	115
Mortality		38.2%		39.9%	

Of 217 delirious patients who received alcohol (practically always in the form of whisky in ounce doses four to six times daily) 83 died or 38.2 per cent., while of 288 such patients not so treated 115 died or 39.9 per cent. The mortality was thus 1.7 per cent. less when alcohol was given. While this decrease in the mortality is not large, we believe that these results render the question whether alcohol should be given to delirious patients one which is most decidedly open to discussion, and not as most writers would have us believe, settled against the use of alcohol.

It should, however, never be withdrawn from cases of incipient delirium tremens. Of 202 such cases on alcohol, 49, or 24.3 per cent. became delirious, while of 500 similar cases deprived of alcohol, 44.6 per cent. became delirious, or 20.3 per cent. more. This clearly shows that while the withdrawal of alcohol may not of itself be sufficient to bring on an attack of delirium tremens in a chronic alcoholic, yet when from other causes the patient is already in the incipient stage, the withdrawal of alcohol greatly increases the chances that he will become delirious.

Ergot. For a number of years Livingston and Lambert have been advocating the use of ergot in chronic alcoholism and Lambert has pointed out the fact that ergot is of great value in the treatment of delirium tremens. Lambert uses ergot hypodermically in Livingston's solution. (One dram solid extract of ergot, one ounce of sterile water, three drops of chloroform, and three grains of chlore-tone. Filter. Dose, 30 drops into the muscles every two to four hours.) He says that "after it there is a distinct tendency to a quieter delirium and less need of restraint, it reduces the tremor, less hypnotic is required and it diminishes the tendency to wet

brain." Since he began the use of ergot in the Bellevue Hospital there has been a marked decrease in the death rate from delirium tremens on his service.

TABLE XX.—Use of Ergot in the First Stage.

		Ergot used.		Ergot not used.	
		Total.	Dev.	Total.	Dev.
First series		72	17	273	128
Second series	Uncomplicated	123	19	161	59
	Complicated	13	4	60	45
		208	40	494	232
Percentage becoming delirious		19.2%		46.9%	

TABLE XXI.—Use of Ergot in the Second Stage.

		Ergot used.		Ergot not used.	
		Total.	Died.	Total.	Died.
First series		80	23	221	109
Second series	Uncomplicated	65	13	82	27
	Complicated	22	12	35	14
		167	48	338	150
Mortality		28.7%		44.3%	

The results in our series fully confirm all that Lambert has said. Of 167 delirious patients on ergot 48, or 28.7 per cent. died, while of 338 similar cases not on ergot 150 died, or 44.3 per cent. It thus appears that the use of ergot decreased the mortality 15.6 per cent. It is equally beneficial in the incipient cases, since only 19.2 per cent. of the cases receiving it developed delirium as compared with 46.9 per cent. among those not getting it.

These results have been obtained by the administration of ergot by mouth, the usual dose being one dram of the fluid extract repeated every four hours. It is evident, therefore, that when it is administered in frequently repeated doses by mouth enough is absorbed to produce definite results. These conclusions are not opposed to the results of the experiments carried out by Croyn and Henderson,²⁵ from which they conclude that pharmacological doses of ergot are ridiculously low, that at least an ounce of any fluidextract should be given by mouth, and that in any case intramuscular injection is to be preferred. They were looking for a sudden and marked effect upon the blood pressure in normal animals, while in delirium tremens the object is to secure a prolonged action upon a disordered circulation, especially the constriction of the dilated arterioles of the brain. Moreover, according to Wood and Hofer,²⁶ the majority of specimens of fluid extract of ergot (6 out of 7) obtained directly from the manufacturer reached a reasonable standard of activity, but deteriorated rapidly especially when kept in unsealed bottles.

²⁵ Jour. of Pharm. and Exp. Therapeutics, August, 1909.

²⁶ Arch. of Int. Med., 1910, vi, p. 3SS.

They conclude that deterioration from age is the chief reason for the unsatisfactory results obtained with the ordinary retail specimens. It is probable that in a hospital where large amounts of ergot are used daily, the drug is reasonably fresh and active. The results of Wood and Hofer also show that the doses recommended by Croyn and Henderson are excessive. No cases of ergotism have come to our attention from this treatment, and Lambert has not observed any at the Bellevue Hospital.

In delirium tremens there is an active hyperemia of the brain and in many cases oedema also. It is reasonable to suppose, and this supposition has been tacitly made in the preceding paragraph, that ergot, which is said to have a selective action on dilated blood-vessels, should produce its effect in delirium tremens by reducing the cerebral hyperemia. It should be remembered, however, that it is not without influence on the general circulation and may be valuable as a stimulant. This last supposition receives some support from the facts mentioned in the next paragraph.

Stimulants were used very rarely and only in moribund cases, so that any consideration of their value is out of the question. Ganscr has called attention to the marked decrease in his death rate from delirium tremens when he began to pay more attention to the circulation; and it seems clear to one examining the records here reported that too little attention was given to this phase of the treatment.

TREATMENT IN THE MASSACHUSETTS GENERAL HOSPITAL. There are certain points which should be mentioned in connection with the cases treated at the Massachusetts General Hospital. These cases quite generally received large doses of hypnotics, hyoscine and morphine being given much more frequently than at the Cook County Hospital. No ergot was used and practically no veronal. In 55 cases in which note was made of the treatment, 35 received morphine, 32 hyoscine, and 5 veronal. As we have already stated, it is not safe to draw conclusions concerning treatment from the mortality in delirium tremens in widely separated hospitals. But it is at least suggestive that the mortality (Table III) was higher at a hospital where the two drugs that gave the worst results at the Cook County Hospital were extensively used and where the two drugs that gave the best results were not employed. In this connection it should be pointed out that in the first series of Cook County Hospital cases (1905 to 1908), where little ergot and practically no veronal were used the mortality (Table III) was 26.4 per cent.; while in the second series (1908 to 1910), where both ergot and veronal were extensively employed, the mortality was 17.5 per cent.

SUMMARY. In conclusion it may be said that medicinal treatment of delirium tremens is much more effective in the first than in the second stage of the disease. Our results would indicate that incip-

ient cases should receive large doses of the hypnotics of which veronal is by far the best, whisky should be given regularly, and ergot administered at frequent intervals either by intramuscular injection or by mouth. Such medication should be discontinued gradually and only after all signs of restlessness and tremor have disappeared. The delirious patient should receive veronal in moderate doses—all other hypnotics and especially morphine and hyoscine should be withheld. Ergot should be given as in the incipient cases. So far as the delirious patients are concerned, our data do not give conclusive evidence whether or not whisky should be regularly employed.

THE CAUSE AND RELIEF OF PAIN IN DUODENAL ULCER.¹

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THE first mention in medical literature of duodenal ulcer is the report of two cases determined post mortem by Mr. Travers² in 1817. The second record is that by an American physician, Irvine, of Philadelphia; but it is to John Abercrombie,³ a Scotch physician, that we must ascribe the priority of noticing the phenomenon that in disease of the duodenum food is taken with relish; that the first stage of indigestion is not interfered with, and that the pain begins about the time the food is leaving the stomach, namely, two to four hours after meals. This was in 1830.

It was not until 1887 that this symptom complex was reëstablished by Bucquoy,⁴ who made the first symptomatic diagnosis which was confirmed at autopsy; the intervening fifty-seven years, containing only records of 143 cases collected from the pathologists and general hospital services where death had ensued from perforation, although in 1852, Wunderlich⁵ mentions a case of death from perforation, in which it is stated that ulcer of the duodenum was suspected previously.

Codivilla,⁶ an Italian surgeon, was the inaugurator of operative interference in cases of chronic non-perforated ulcer of the duodenum, when he demonstrated the efficacy of a gastro-enterostomy in this condition on March 22, 1893, and again on May 5, 1898.

¹ Read before the American Gastro-Enterological Association, April, 1911.

² *Medico-Chir. Trans.*, London, viii, 232.

³ *Path. and Pract. Research of Dis. of the Stomach.*, Edinburgh, 1830, pp. 103, etc.

⁴ *Arch. gén. de méd.*, 1 to 398 et seq.

⁵ *Handbuch der Path. und Therap.*, 111 to 175.

⁶ *Sei Casi Gastroenterost. Sperimentale. Mem. Orig.* Firenze, 1893, pp. 406 to 421, and *Contrib. alla chirug. gastrica.*, Bologna, 1898.

At first we were in the transition period between the epochs of surgery based on anatomy and that grounded on pathology, which latter has only been elaborated since Virchow, after the middle of the nineteenth century, brought forward his observations.

Now a new era has opened. Surgery based on physiology and its developments may be included within the past decade. It is to offer a contribution to this beginning epoch that I wish to present the following observations:

I have had the opportunity of examining personally previous to operation one hundred cases on whom an operation later by Dr. William Mayo confirmed the diagnosis of duodenal ulcer. The privilege of reporting the results of my study of these has been given me by the operator. In the present paper I wish to consider only those clinical points relevant to the time element of the occurrence of the pain, the method employed to relieve it, the promptness of its relief, and the degree of total acidity of the gastric juice.

The average time of the onset of epigastric distress in this series of consecutive cases, was between three and four hours after meals. Almost without exception the ingestion of any substance, water, alkalies, milk, cracker, beer, and even acids, caused the pain to stop immediately. Probably the diagnostic point of greatest significance that can be considered in relation to this phenomenon is the observation elicited from the patient that he usually goes to bed with some form of food or liquid beside him, as he knows that he will be awakened at a definite time and can only get to sleep again by taking a mouthful or two of the substance, which he has found from experience, will give him immediate relief, and, as briefly indicated above, his fancies may lead him to partake of the most bizarre things. So regular and unfailing are these occurrences that the term "clocksetters" has been applied to them, and, from that single word we should be able to make a correct diagnosis in possibly 90 per cent. of the cases presenting this symptom.

I have made complete pre-operative stomach analyses of all of these cases, and find that the average total acidity is 77, and determined that in approximately 70 per cent. there was a hypersecretion of this hyperacid juice. This fact is further confirmed by the subjective history that in nearly all cases the patients complain of sour, acrid, bitter, or burning eructations of a mouthful or two of stomach contents between meals, which, as they express it, "sets their teeth on edge;" and, indeed, it is so concentrated, that in many instances it has been corrosive in its action on the teeth, giving strong confirmatory evidence in the diagnosis of this condition.

As has been so plainly demonstrated by Edkins and Tweedy,⁷

the production of gastric juice subsequent to the ingestion of a meal is after a time effected through the agency of the gastric hormone obtained from the pyloric mucosa, and in order to complete the preparation of a moderate mass the hydrochloric acid must be secreted in very considerable quantity; in fact, a much greater amount than is recoverable during the first hour. This conclusion is easily demonstrated by an analysis of a complex meal, if it be extracted during the third hour, or just as it is about to pass into the duodenum, when the acidity will be found to average between one and two hundred, or even higher.

It may then be considered even more than an inference that after the food has left the stomach entirely there is still an outpouring of hydrochloric acid, and in cases of duodenal ulcer this would seem to be greater in amount and concentration than is ordinarily the case—if I have been correct in my interpretation of the stomach analyses. This would seem to place the inferential conclusions that the pain was caused by the irritation of the ulcer by hydrochloric acid on a fairly firm chemical as well as clinical basis.

One other factor must be taken into consideration, namely, may not the pain be caused by spasm of the pylorus? This is by some accepted as the explanation. As bearing upon the possibility of this being the cause, the following observations should be carefully considered:

If pyloric spasm was the etiological factor, the pain would be irregular in its onset; if food had any effect, it would be to increase the discomfort, rather than diminish it. In muscular spasm of the gastric outlet the distress is more indefinite, of less intensity, of shorter duration than that found in typical duodenal ulcer, and its radiation, if any, is downward toward the umbilicus, a phenomenon so characteristic of appendicular gastralgia, which is pylorospasm. Further, I have not seen demonstrated at operation very many instances of this peculiar unmistakable contraction of the pylorus in cases of duodenal ulcer, while it is perfectly demonstrable in the large majority of instances when the gastric discomfort emanates from the appendix or gall bladder. Finally, the two peculiar types of epigastric distress are occasionally found in the same patient, at the same time, two distinct subjective sensations. It will frequently be described as a steady burning, accompanied by a grinding, boring, irregular pain, and on taking food or drink the former is relieved, while the latter is temporarily unaltered.

If these hypotheses are correct, then the most plausible explanation for the control of the pain by the ingestion of food, etc., would be that this secretion was in some manner neutralized. To determine what this agent was, the following experiments were carried out for the purpose of ascertaining more definitely the physical and chemical properties of the duodenal secretion, if, indeed, there

was any such fluid, and what effect reflex stimulation, from placing food in the stomach, would have on it. Ten adult dogs, averaging between twelve and fifteen pounds, were taken, and the following operative procedure was done on each (see figure):

1. Ligature of the pylorus.
2. Ligature of the duct of Wirsung.
3. Ligature of the duct of Santorini.
4. Ligature of the common bile duct.
5. Gastro-enterostomy 30 cm. from pylorus.
6. Cholecystostomy.
7. Ligature of the duodenum 15 cm. from pylorus.
8. Duodenostomy.

By these procedures it resulted that no extraneous secretion could enter the duodenum, while the secretion of the duodenum proper was prevented from escaping into the intestine below. By the final duodenostomy the recovery of the pure duodenal secretion was provided for.

In every instance the postoperative course was uneventful until between the fiftieth and sixtieth hours, when all the dogs died a "physiological death," due to the exclusion of the duodenal secretion from the remainder of the intestinal canal, as has been so perfectly demonstrated lately by Matthews,⁸ and which was previously intimated by Maury.⁹

Twenty-six analyses were made, in some instances two, in others as many as five, of the secretion gathered from the duodenostomy tube. These showed an average alkalinity of 77, being titrated against an $\frac{N}{10}$ H_2SO_4 solution, using methyl orange as an indicator.

The duodenal secretion was obtained in every instance entirely free from pancreatic juice and bile, and in many of the specimens there was no mucus. The duodenal secretion thus obtained is of a light straw color, very slightly turbid (due to lymphocytes), is practically odorless, but decomposes very rapidly. It has a constant specific gravity of between 1006 and 1009 by weight, and is secreted on a starving stomach in quantities averaging between three and four hundred cubic centimetres, every twenty-four hours, it has practically negative digestive properties.

After determining what these factors were for each dog, without any stimulation or food or water, these elements were introduced to see what effect they might have on this secretion. In two instances the dogs were allowed to smell well-cooked meat, with the result that the secretion was markedly stimulated, *i. e.*, previous to experiment they were secreting 10 c.c. per hour; two minutes after smelling meat, 13 c.c. spurted out of the tube in one instance, in the other, about 5 c.c. was gathered within four minutes.

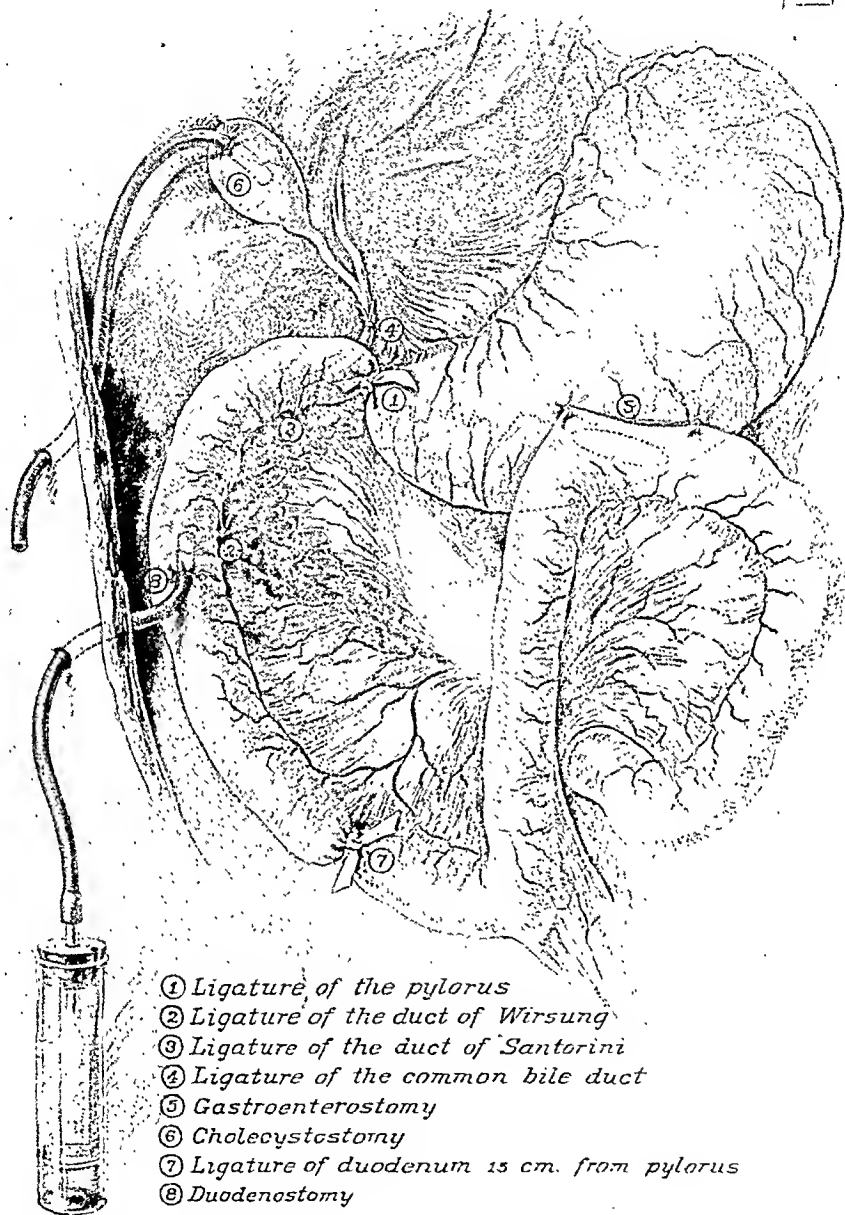
⁸ Jour. Amer. Med. Assoc., 1910, iv, 293.

⁹ AMER. JOUR. MED. SCI., 1909, cxxxvii, 725.

Water was given at regular intervals (the dogs drinking with avidity, when allowed), and in *every* instance they secreted as

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Illustrating the method devised to obtain pure duodenal secretion. The operative procedures should be undertaken in the order indicated by the numerals.

much within five minutes as they had during the preceding hour, and if allowed to drink at will continued an increased secretion all day.

Strong beef tea was next introduced through a stomach tube, being retained usually about five minutes before it was regurgitated, during which time the duodenal secretion was more markedly stimulated than in either of the preceding series, and continued so for some time after having vomited the liquid. They refused in every instance to eat any food, so I was unable to make any other observations which would have been of interest.

This excess of secretion was of slightly lower alkalinity and one or two points lower in specific gravity, but for all practical purposes identical with that secreted previously. That it was stimulated through nerve reflexes hardly admits of question, as the duodenum was imperviously constricted at the pylorus and proximal to the gastro-enterostomy. That it was a pure secretion from the duodenal mucosa is evident, owing to the fact that the bile and pancreatic ducts were all ligated off securely. That it was not a transudation of the serum or lymph is indicated, because of its having a radically different specific gravity from any other known body fluid.

The absolute evidences of its stimulation being effected through the ingestion of any substance, and even through psychical reflexes, and its chemical properties, are too pertinent to lead us to believe that we are dealing with a mere coincidence. The cause of death in these dogs and the pathology of the organs in each case coincide strikingly with that noticed in human beings under similar circumstances. Some facts observed bearing upon the cause of death in cases in which the duodenum is involved I hope to have the opportunity of presenting at some later date.

From a study of the above, however, I feel justified in concluding that:

A. The cause of pain in duodenal ulcer is the hydrochloric acid contained in the gastric juice coming in contact with the ulcerated surface after it has passed into the duodenum. This conclusion is based on the following observations: (1) Ulcer of the duodenum reflexly excites a hyperacidity of the gastric juice; (2) the maximum amount of secretion of hydrochloric acid in the stomach is due to a direct chemical action (hormones) and is at its height from one to four hours after meals; (3) it passes into the duodenum as hydrochloric acid, there being no food for four hours after meals for it to work upon; and (4) it does not excite a flow of the duodenal juice directly, and is not neutralized by the small amount present.

B. The relief of pain in duodenal ulcer follows the ingestion of any substance into the stomach, and is due to a reflex stimulation of the duodenal secretion which neutralizes the acid gastric juice. This conclusion is based on the following facts already demonstrated in the above experiments: (1) Food taken into the stomach excites at once a reflex secretion in the duodenum; (2) the duodenal secretion is alkaline in approximately the same degree as the gastric

juice is acid; and (3) this secretion is of sufficient quantity and concentration to neutralize the hydrochloric acid of the gastric juice.

These experiments were undertaken in the Hull Laboratories at the University of Chicago, under the direction and with the co-operation of Dr. S. A. Matthews.

THE COMPLEMENT-FIXATION TEST IN THE DIAGNOSIS OF GONOCOCCIC INFECTIONS.¹

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To Müller and Oppenheim,² in 1906, belongs the credit of first applying the complement-fixation test to the study of the serum of a patient having gonorrhoeal arthritis. This serum gave a positive reaction, and the serum of a patient suffering from disease not gonorrhoeal gave a negative reaction, thus proving that gonorrhoeal serum contains a specific antibody for the gonococcus. Further data were published by Bruck³ later in 1906, and by Meakins,⁴ Vannod,⁵ and Wollstein,⁶ in 1907. Teague and Torrey⁷ also published a report in 1907 confirming the fact that all antigonococcic sera have the power to bind complement; but when several different strains of gonococci are used, strain "A" only reacts strongly with the serum from a rabbit immunized with strain "A;" and strain "B" only with the serum of a rabbit immunized with strain "B," and so on, which would seem to prove Torrey's contention that there are several different types of gonococci. An exhaustive report, including the study of a number of human and immunized rabbit sera, was published by T. Watabiki⁸ in January, 1910, in which he confirmed the work of the previous investigators in its essential points.

During the last few months we have applied the complement-fixation test to a total of 324 human sera. These sera were taken

¹ Read at a meeting of the New York Academy of Medicine, Section on Medicine, October 18, 1910.

² Wien. klin. Woch., 1906, No. 19, p. 894.

³ Deut. med. Woch., 1906, No. 70, p. 36.

⁴ Johns Hopkins Hosp. Bull., 1907, No. 18, p. 255.

⁵ Zentrbl. f. Bakter., 1907, No. 44, p. 10.

⁷ Jour. Med. Res., 1907, No. 17, p. 223.

⁶ Jour. Exper. Med., 1907, No. 9, p. 588.

⁸ Jour. Inf. Dis., 1910, No. 7, p. 159.

from persons of both sexes having acute or chronic gonorrhœal infection; from others having no history or clinical manifestations of gonorrhœa, and from patients suffering from various diseases other than gonorrhœa. The tests have all been carried through in duplicate, using both the antisheep and Noguchi's antihuman hemolytic systems.

The chief point of departure from the methods of previous investigators in this line has been in the use of many different strains of gonococci in the preparation of the antigen, instead of only one. We were led to do this by the knowledge that different strains of the gonococcus seemed to differ considerably one from another, and the possibility suggested itself that perhaps the serum of a patient infected with one strain of the gonococcus might only fix complement in the presence of an antigen from the same strain, or from some closely allied strains, but might not do so in the presence of an antigen prepared from some widely separated strain. In case we proved this point we realized that the method would be too cumbersome for clinical application if all of the sera had to be tested against separate antigens prepared from a number of different strains of gonococci.

The idea occurred to us that possibly an antigen prepared from a mixture of all the different strains might work satisfactorily; in other words, that a "polyvalent" antigen might detect the presence of gonococcal antibodies every time that a single strain would do so. If so, the technique would be much simplified. These points were taken up and we consider proved by our experimental work, which will be given in detail later. Here we think it is best to describe our technique and the preparation of material.

In our work we have used both the antisheep and antihuman hemolytic systems, and have followed the technique as laid down in the well-known Wassermann test for syphilis, and in Noguchi's modification of the Wassermann test. We would, however, say that in employing the antihuman system we have invariably used *inactivated* patients' serum. The preparation and titration of the amboceptor, complement, and red blood cell suspension for the two systems has been so frequently described that we do not think it necessary to enter into the details here.

PREPARATION OF THE ANTIGEN. 1. In the preparation of the antigen, from nine to twelve different strains of gonococci have been used at various times.

2. To from twenty-four- to forty-eight-hour-old cultures of gonococci grown on Tholman's media, containing 2 per cent. of glucose, 2 c.c. of sterile 0.85 per cent. saline solution to each tube was added and the growth of cocci scraped off the surface of the media with a platinum loop.

3. The resulting suspension of cocci in saline was then decanted into a sterile bottle and placed in an inactivating oven at a temperature of 56° C. for thirty minutes; it was then placed in a shaker

and agitated for twenty-four hours, after which it was centrifugated; the supernatant fluid was then pipetted off and placed in a tightly corked sterile bottle, a capillary drop of lysol being added as a preservative. This was placed in the ice chest until required for tests.

Some recent experiences have led us to believe that possibly a better antigen might be obtained by allowing the suspension of cocci in the saline to remain for several hours without shaking, at a temperature of about 37° C., as a more thorough extraction seems to take place by so doing.

For the titration of the antigen we have used as a positive control either the serum of a patient who has been treated with injections of dead gonococci, or else Torrey's antigenococcic serum, as prepared by Parke, Davis & Co. This is serum from an animal which has been immunized against many different strains of gonococci. The quantity of antigen to be used is the quantity that will completely inhibit hemolysis of the given suspension of red blood cells in the presence of definite quantities of positive serum and complement; provided that double this amount does not interfere with complete hemolysis of the cells, using a normal serum and complement. Our daily routine is as follows:

1. Titration of the complement with the given quantity of red blood cell suspension and given quantity of an amboceptor of known hemolytic strength, the object of this being to determine the exact complement value of the guinea-pig serum used. Careful estimation of the exact quantities of amboceptor and complement to be used is of the greatest importance if accurate and reliable results are to be obtained.

2. Titration of antigen against a positive serum. This procedure gives us known quantities of amboceptor, complement, antigen, and red blood cell suspension

The technique of the day may be graphically depicted as follows, using the antisheep hemolytic system in a positive case.

TABLE I.

Patient's serum.	Antigen.	Complement 10 per cent.	Amboceptor	Sheep's red blood cells 5 per cent.	Hemolysis.
0.15 c.c.	0	0.05 c.c.	0.05 c.c.	0.05 c.c.	Complete
0.10 c.c.	0	0.05 c.c.	0.05 c.c.	0.05 c.c.	Complete
0.05 c.c.	0	0.05 c.c.	0.05 c.c.	0.05 c.c.	Complete
0	Double titrated quantity	0.05 c.c.	0.05 c.c.	0.05 c.c.	Complete
0	0	0.05 c.c.	0.05 c.c.	0.05 c.c.	Complete
0	0	0	0.05 c.c.	0.05 c.c.	None
0	0	0.05 c.c.	0	0.05 c.c.	None
0.15 c.c.	Titrated quantity	0.05 c.c.	0.05 c.c.	0.05 c.c.	None
0.10 c.c.	Titrated quantity	0.05 c.c.	0.05 c.c.	0.05 c.c.	None
0.05 c.c.	Titrated quantity	0.05 c.c.	0.05 c.c.	0.05 c.c.	None
Positive serum					
0.10 c.c.	Titrated quantity	0.05 c.c.	0.05 c.c.	0.05 c.c.	None
0.10 c.c.	0	0.05 c.c.	0.05 c.c.	0.05 c.c.	Complete

TABLE II.—*Experimental Work.*

Titration of various strains of gonococci, separately, and mixture of all the strains against Torrey's antigenococcic serum.

Quantities of antigen used.		G	L	Q	C	O	K	B	J	A	Mixture of 9 strains.	Quantities of serum used.	
		0.1	0	0.1	0	0.1	0	0.1	0	0.1	0		0.1
0.2	c.c.	0	c	0	c	0	c	0	c	0	c	0	c
0.15	c.c.	0	c	0	c	0	c	0	c	0	c	0	c
0.1	c.c.	0	c	0	c	0	c	0	c	0	c	0	c
0.08	c.c.	0	c	0	c	0	c	0	c	0	c	0	c
0.06	c.c.	0	c	0	c	0	c	0	c	+	c	0	c
0.04	c.c.	0	c	0	c	0	c	0	c	+	c	+	c
0.02	c.c.	0	c	0	c	0	c	0	c	+	c	+	c
0.01	c.c.	0	c	0	c	0	c	0	c	+	c	+	c
0.005	c.c.	c	c	c	c	c	c	c	c	c	c	+	c
0.0025	c.c.	c	c	c	c	c	c	c	c	c	c	c	c
0.00125	c.c.	c	c	c	c	c	c	c	c	c	c	c	c
0		c	c	c	c	c	c	c	c	c	c	c	c

0 = no hemolysis.
++ = moderate hemolysis.

+ = slight hemolysis.
c = complete hemolysis.

TABLE III.

Titration of Torrey's serum (P., D. & Co.), against previously determined quantities of antigen.

Quantities of serum.		Hemolysis with strains.									Mixture of all 9.
		A	J	O	G	K	C	L	B	P	
		0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.
0.1	c.c.	0	0	0	0	0	0	+	+	+	0
0.05	c.c.	0	0	+	0	0	0	++	+	++	0
0.025	c.c.	0	+++	++	0	0	0	+++	++	++	0
0.01	c.c.	+	+++	c	++	0	0	c	+++	+++	+
0.005	c.c.	++	+++	c	++	0	+	c	+++	+++	+
0.0025	c.c.	++	+++	c	+++	0	+	c	o	c	++
0.001	c.c.	+++	+++	c	c	+	++	c	c	c	c
0		c	c	c	c	c	c	c	c	c	c

0 = no hemolysis. + = slight hemolysis. ++ = moderate hemolysis.
 +++ = considerable hemolysis. c = complete hemolysis.

This shows how differently the various antigens prepared from single strains fix complement in the presence of serum from an artificially highly immunized animal. Presumably the animal received only small quantities of L. B. and P. strains or allied ones.

TABLE IV.

Titration of separate strains and mixtures against the serum of rabbit immunized as follows: (1) inoculation strains K and G; (2) inoculation strains K and G; (3) inoculation strains K, G, and Q; (4) inoculation strains K, G, and O; (5) inoculation strains K, G, Q, and C.

Quantities of antigen used.	G		L		Q		C		O		K		T		Mixtures of 7.		Quantities of serum used.
	0.1	0	0.1	0	0.1	0	0.1	0	0.1	0	0.1	0	0.1	0	0.1	0	
0.3 c.c.	c	c	c	c	c	c	c	c	c	c	c	c	c	c	++	c	
0.25 c.c.	+	c	c	c	c	c	c	c	c	c	++	c	c	c	0	c	
0.2 c.c.	0	c	+	c	c	c	0	c	c	c	0	c	c	c	0	c	
0.15 c.c.	0	c	++	c	c	c	0	c	c	c	0	c	c	c	0	c	
0.1 c.c.	0	c	+++	c	+	c	0	c	c	c	0	c	c	c	++	c	
0.08 c.c.	+	c	+++	0	+	c	0	c	c	c	+	c	c	c	c	c	
0.06 c.c.	++	c	+++	c	+	c	+	c	c	c	++	c	c	c	c	c	
0.04 c.c.	c	c	+++	c	++	c	+++	c	c	c	++	c	c	c	c	c	
0.02 c.c.	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	
0.01 c.c.	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	
0	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	

In the higher quantities the antigen showed lytic qualities.

Strong positive results were obtained with the antigen prepared from strains K, G, and C, and from the mixture of the seven strains (Torrey considers K and C strains to be closely allied.) Poor fixation was obtained with strains L and Q, and none with strains O and T.

Good fixation was obtained with strains N, B, and A and the mixtures; good fixation could not be obtained with strains H, I, and J; quantities giving good fixation with a positive serum also interfered with hemolysis to a certain extent when no positive serum was added. This was especially the case with strains I and J.

Perfect fixation of the complement was only obtained with strains N, I, J, and A, and the mixture of all twelve strains; strains K, C, B, and H gave imperfect fixation, and strains O, G, L, and Q none. This shows conclusively that (1) if only a single strain is used in the preparation of the antigen many negative results would be obtained in positive cases, and (2) that a polyvalent antigen fixes complement when a single strain does.

In Case I a positive result was obtained only with strains H and J; Case II, only with strain H; Case III, only with strain J; Case IV, only with strains H and J; Case V, only with strains G and L; Case VI, only with strains C, B, A, K, and O. The antigen prepared from the mixture of all the strains always gave a positive result.

TABLE VI.

Testing serum of rabbit immunized to gonococcus culture, strain A, against antigens prepared from the various strains and their mixtures; the quantities of these to be used having been previously determined by titration. Hemolysis with strain.

Quantity of serum.	O 0.05	G 0.05	L 0.05	Q 0.05	K 0.05	C 0.05	B 0.05	H 0.05	N 0.05	I 0.05	J 0.04	A 0.02	Mixtures of twelve.
0.1	c	c	c	c	++	++	++	++	0	0	0	0	0
0	c	c	c	c	c	c	c	c	c	c	c	c	c

TABLE VII.

Testing of clinical cases, giving a positive reaction, against antigens prepared from separate strains and from mixtures of all strains; the quantities of each antigen to be used having been previously determined by titration against a polyvalent antigenococcic serum.

Strain.	Case I.	Case II.	Case III.	Case IV.	Strain.	Case V.	Strain.	Case VI.
N	++	+++	c	++	T	c	C	0
B	c	c	c	c	O	c	B	0
H	0	+	c	0	K	+++	L	++
I	++	c	c	c	C	+++	A	0
J	0	++	0	c	Q	+++	K	0
A	c	++	c	c	G	0	O	0
Mixture of 12	0	0	0	0	L	0	J	++
No antigen	c	c	c	c	Mixture of 7 No antigen	0 c	Mixture of 7 No antigen	0 c

The results given above would seem to justify the following conclusions:

1. That the different strains of the gonococcus differ markedly one from another—so much so that the antibodies produced in the body by the toxin of one strain will in many instances not bind complement in the presence of an antigen prepared from another strain. Therefore, if only one strain is used in the preparation of the antigen, a great many negative results would be obtained in positive cases.

2. An antigen prepared from many strains fixes complement whenever one of its component strains does so, and consequently the necessity of testing a serum against a number of antigens separately is avoided. It is not to be denied that there probably are other strains of gonococci differing widely from any present in the polyvalent antigen, so that at times a negative result will be obtained in a positive case.

We consider, however, that working with an antigen composed of many strains, one will obtain a positive reaction in the great

majority of cases of gonococcal infection, and the use of the polyvalent antigen simplifies the procedure so that it can be of practical value for diagnostic purposes.

We have, in addition, tested the polyvalent antigen against the serum of animals immunized to the following varieties of bacteria: *Bacillus typhosus*, *Bacillus dysenteriae*, *Bacillus diphtheriae*, *Bacillus pyocyaneus*, *Bacillus tetani*, streptococcus, and living and dead meningococcus, with uniformly negative results. The only positive result obtained was with Flexner's antimeningococcic serum. We have not had the opportunity to examine the serum of patients suffering from cerebrospinal meningitis, but even if a positive reaction is obtained in this disease, we do not think it will detract from the practical value of the test, as there could be very little doubt of the diagnosis in such cases. We have further examined the sera of patients suffering from pneumococcus and micrococcus catarrhalis infection, with negative results.

ANALYSIS OF TESTS ON CLINICAL CASES. The great majority of these cases were tested with an antigen prepared from twelve different strains of gonococci, as furnished us by the courtesy of Dr. John Torrey, of the Loomis Laboratory. At times, for a brief period, we had to use an antigen prepared from only six strains of gonococci. At such times our results did not seem to be as accurate as when we used the twelve-strain antigen. Several cases which gave negative results with the six strains gave definite positives when tested afterward with the twelve-strain antigen. The greater the number of strains of gonococci used in the preparation of the antigen the more accurate will be the results.

Acute Gonorrhæal Urethritis.

	Positive.	Negative.
(a) Duration, 3 days to 3 weeks	0	5
(b) Duration not stated	1	0
Acute urethritis, gonococci not found	0	1

Chronic Urethritis of Gonorrhæal Origin.

	Positive.	Negative.
1. Gonococcus present.		
Case I. Duration 6 months.	1	0
Case II. Duration 2 years; profuse discharge; gonococci abundant	1	0
Case III. Duration 13 years	1	0
Case IV. First attack 12 years ago; one week ago noticed very slight discharge containing a few extracellular gonococci; prostate negative	1	0
2. Gonococci not found.		
Case I. Duration 2 years; first attack	1	0
Case II. Duration 7 weeks; first attack	1	0
Case III. Duration several years; gleet discharge present; first attack	0	1
Case IV. Duration 5 months; sometimes has glycerin-like drop; no treatment for two months	1	0
Case V. Duration 10 months; first attack	1	0
Case VI. Duration 15 months; first attack	1	0
Case VII. Duration 10 months; first attack	1	0
Case VIII. Duration 2 years; first attack	1	0
Case IX. Duration 16 months; first attack	1	0

Chronic Urethritis of Gonorrhæal Origin.

		Positive.	Negative.
Case	X. Duration 1 year; first attack; at present has serous discharge which does not yield to treatment	1	0
Case	XI. Duration 2 months; at present has occasional discharge in the morning; anterior urethra alone affected; first attack	0	1
Case	XII. Duration 2½ years; first attack; has had recurring discharge off and on.	0	1
Case	XIII. Duration 2 months; has had previous attack	1	0
Case	XIV. Duration 9 months; has had previous attack	1	0
Case	XV. Duration 3 years; has had previous attack	1	0
Case	XVI. Duration 7 months; has had previous attack	1	0
Case	XVII. Duration 6 months; has had previous attack	1	0
Case	XVIII. Duration 5 months; has had previous attack	1	0
Case	XIX. Duration, morning drop for three years; has had previous attack	0	1
Case	XX. Duration, chronic relapsing urethritis for 13 years; has had previous attack	1	0
Case	XXI. Duration, relapsing urethritis for 10 years; has had previous attack	1	0
Case	XXII. Duration, gonorrhœa 10 years ago, and has had several attacks since; at present has morning drop; prostate apparently well	0	1
Case	XXIII. Duration 2 years; no statement of previous attack; has morning drop	1	0
Case	XXIV. Duration 9 months; no statement of previous attack; recent discharge	0	1
Case	XXV. Duration 3 years; no statement of previous attack; pasting of meatus at times and pain at end of penis when urinating	1	0
Case	XXVI. Duration not stated; no statement of previous attack	0	1
Case	XXVII. Duration 1½ years; no statement of previous attack	1	0
Case	XXVIII. Duration 3 years; no statement of previous attack	1	0
Case	XXIX. Duration 4 years; no statement of previous attack.	1	0
Case	XXX. Duration 1½ years; no statement of previous attack; morning drop; prostate apparently well	0	1
Case	XXXI. Duration 7 months; no statement of previous attack	0	1
Case	XXXII. Duration 10 months; no statement of previous attack	1	0
Case	XXXIII. Duration 2½ years; no statement of previous attack; stricture; anterior urethra	1	0
Case	XXXIV. Duration 10 months; no statement of previous attack	1	0
Case	XXXV. Duration 3 years; no statement of previous attack	1	0
Case	XXXVI. Duration 4 years; no statement of previous attack; discharge at night time only	1	0
3. No examination made for gonococci, but serum was taken from cases in stage when gonococci are usually absent.			
Case	I. Duration 9 months; first attack	1	0
Case	II. Duration 2 months; first attack	1	0
Case	III. Duration 10 months; has had previous attack	0	1
Case	IV. Duration 2 months; has had previous attack	1	0
Case	V. Duration 1 week; has had previous attack	1	0
Case	VI. Duration, no statement; relapsing	1	0
Case	VII. Duration, no statement; pus and shreds in urine	1	0
Case	VIII. Duration, no statement	1	0

Chronic Urethritis; History of Gonorrhœa Doubtful.

		Positive.	Negative.
Case	I. Pus and shreds in the urine	0	1
Case	II. Sick 4 years; apparently no gonorrhœa; has urethral discharge, with cloudy urine	0	1
Case	III. Urinary trouble for 1½ years (Gonorrhœal?). Had epididymitis seven years ago	1	0
Case	IV. Has had discharges for 5 weeks; no gonococci have been found	0	1

Chronic Prostatitis.

1. Having gonorrhœal history; gonococci absent in all unless specifically stated to be present.

		Positive.	Negative
Case	I. History of infection 3½ years ago	0	1
Case	II. History of infection 6 years ago; neurasthenic	0	1
Case	III. History of infection 6 years ago	1	0
Case	IV. History of infection 2 years ago	0	1
Case	V. History of infection 3 years ago; prostatitis and vesiculitis now; colon bacillus present	1	0
Case	VI. History of infection 9 years and 2½ years ago	1	0
Case	VII. History of infection 10 months ago	1	0
Case	VIII. History of infection 7 months ago	0	1
Case	IX. History of infection 4 years ago	1	0
Case	X. History of infection 3 years ago	1	0
Case	XI. History of infection 1½ years ago	1	0
Case	XII. History of infection—four attacks in 1½ years, the last one 5 months ago	1	0
Case	XIII. History of infection—three attacks in 4 years, the last one 9 months ago	0	1
Case	XIV. History of infection—three attacks in 3 years, the last one 9 months ago	1	0
Case	XV. History of infection 16 months ago	1	0
Case	XVI. History of infection 2 years ago; urine cloudy	1	0
Case	XVII. History of infection 10 months ago	1	0
Case	XVIII. History of infection 6 months ago; cocci present	1	0
Case	XIX. History of infection 15 months ago	1	0
Case	XX. History of infection 10 months ago	1	0
Case	XXI. History of infection 13 and 12 years ago; operation on the kidney 12 years ago; external urethrotomy one year ago; had blood in the urine at that time	0	1
Case	XXII. History of infection 3 years old; occasionally has discharge; test made with 6 strain antigen was negative; test repeated with 12 strain antigen	1	0
Case	XXIII. History of infection 7 years ago; prostatic trouble since	1	0
Case	XXIV. History of infection not stated; chronic prostatitis; no gonococci found; urine contains pus and shreds; has morning drop	0	1
Case	XXV. History of infection 3 years ago; urine clear; no gonococci present; (was tested 7 months before and gave a positive reaction (V), Case XVI	0	1

Chronic Prostatitis.

2. History of gonorrhœa doubtful.

		Positive.	Negative.
Case	I.	0	1
Case	II.	1	0

Sterility.

Having history of gonorrhœal infection.

		Positive.	Negative.
Case	I. History of infection 5 years ago	0	1
Case	II. History of infection 9 years ago	1	0
Case	III. History of infection 10 years ago	0	1

Epididymitis.

1. Having gonorrhœal history.

		Positive.	Negative.
Case	I. History of infection 2 years ago	1	0
Case	II. History of infection 3 years ago; recurring knuckle in epididymis	1	0
Case	III. History of infection 5 years ago; relapsing epididymitis; pain in back and groin and urethra; had chronic prostatitis; no discharge present; no cocci for 4 years, but gets epididymitis after instrumentation	0	1

2. Gonorrhœa denied.

Case	I. Duration of disease 2 weeks	0	1
Case	II. Duration of disease not stated	0	1
Case	III. Duration of disease 2 years; thickening of epididymis; frequent urination; nocturnal micturition; stricture	1	0
Case	IV. Duration of disease 1 week	0	1

Verumontanum Cases.

1. Having gonorrhœal history—gonococci absent in all at time of test.

		Positive.	Negative.
Case	I. History of infection 4 years ago; discharge still present	1	0
Case	II. History of infection not stated	1	0
Case	III. History of infection 10 months ago	1	0
Case	IV. History of infection—first infection 12 years ago; second infection 3 years ago	1	0
Case	V. History of infection—four attacks	1	0
Case	VI. History of infection 2 years ago	1	0
Case	VII. History of infection—3 attacks in 14 years; last one 7 years ago	0	1
Case	VIII. History of infection 4 years ago; impotent	1	0
Case	IX. History of infection 2½ years ago	1	0
Case	X. History of infection 4 years ago; well for 3 years, when endoscope was used and gonococci appeared; no gonococci at present. Verumontanum(?)	0	1
Case	XI. History of infection—first infection 4 years ago; second infection 2 years ago; at present has verumontanum trouble	1	0
Case	XII. History of infection 1½ years ago; now has verumontanum trouble	0	1
Case	XIII. History of infection 2 years ago; has morning drop; at present treated for verumontanum trouble	1	0
Case	XIV. History of infection 15 years ago; has had about ten attacks since; no gonococci found for long time	0	1
Case	XV. History of infection 1½ years ago	0	1
Case	XVI. History of infection 12 years ago	0	1
Case	XVII. History of infection 3 years ago; profuse discharge brought on by instrument examination	1	0
Case	XVIII. History of infection 2 years ago	1	0

2. Gonorrhœa doubtful or denied.

Case	I. Verumontanum case pure and simple; getting well under treatment through urethroscope; had massage of prostate for two years without benefit; for 7 years has had pasting of lips of the meatus; never had gonorrhœa	0	1
Case	II. Doubtful history of having had gonorrhœa 2 years ago	0	1
Case	III. Denies gonorrhœa	1	0
Case	IV. Test repeated on Case III	1	0
Case	V. Rheumatic and verumontanum trouble for 3 years	0	1
Case	VI. Has had verumontanum trouble for 2½ years	0	1

Miscellaneous Cases.

Having no history of gonorrhœa.

		Positive.	Negative.
Case	I. Sick 4 years; rheumatic pains, relieved by serum or bacterins	0	1
Case	II. Sick 8 months; has practised coitus interruptus.	0	1
Case	III. Sick 2½ years; masturbator; stricture of anterior urethra	0	1
Case	IV. Masturbator; impotent	0	1
Case	Y. Masturbator for 3 years	0	1

Controls.

Sixteen cases having no signs or history of gonorrhœa—all negative.

Clinically Cured Cases of Gonorrhœa.

		Positive.	Negative.
Case	I. Gonorrhœa 4 or 5 years ago; has a few shreds	1	0
Case	II. Gonorrhœa 20 years ago.	1	0
Case	III. Gonorrhœa 6 years ago; second attack 4 months ago	0	1
Case	IV. Gonorrhœa—first attack 3 weeks ago; no discharge for past 2 days	0	1
Case	V. Gonorrhœa—first attack 6 years ago, lasting 3 weeks; second attack 3 years ago, lasting 3 months; slight impotency for past 3 weeks	0	1
Case	VI. Gonorrhœa 9 or 10 years ago; no signs present now	1	0
Case	VII. Gonorrhœa—first attack 6 years ago; second attack 2 years ago; verumontanum case apparently cured	0	1
Case	VIII. Gonorrhœa 18 years ago and 4 years ago; treated for verumontanum trouble and impotency; cured 2 years ago	1	0
Case	IX. Gonorrhœa 5 years ago; had stricture and verumontanum trouble; now apparently well	1	0
Case	X. Gonorrhœa 4 years ago	0	1
Case	XI. Gonorrhœa 6 years ago; now apparently well, but complains of pains in knees; looks neurasthenic	1	0
Case	XII. Gonorrhœa 18 years ago	1	0
Case	XIII. Gonorrhœa 3 years ago; apparently well; no gonococci found in prostatic fluid	1	0
Case	XIV. Gonorrhœa 1 year ago	1	0
Case	XV. Gonorrhœa 2 years ago; question of cure	1	0
Case	XVI. Gonorrhœa 3 years ago; no apparent gonorrhœa at present; has pains in rectum and legs	0	1
Case	XVII. Gonorrhœa 8 months ago; seems well now	0	1
Case	XVIII. Gonorrhœa 4 months ago; seems well now	0	1
Case	XIX. Gonorrhœa 5 months ago; seems well now	1	0
Case	XX. Gonorrhœa 5 years ago; at times has burning sensation in urethra; neurasthenic	0	1
Case	XXI. Gonorrhœa—duration not stated; has had posterior urethritis; now apparently well	1	0
Case	XXII. Gonorrhœa 5 years ago; no evidence now; burning in urethra at times; neurasthenic; vesiculotomy done without benefit	1	0
Case	XXIII. Gonorrhœa 3 years ago, lasting 4 months; no symptoms or signs since	0	1
Case	XXIV. Gonorrhœa 7 years ago and twice since; no discharge for 4 months	0	1
Case	XXV. Gonorrhœa, many attacks during the last 10 years; apparently well now	1	0
Case	XXVI. Gonorrhœa, multiple attacks during the last 10 years; last one 3 years ago	0	1
Case	XXVII. Gonorrhœa, chronic, 7 years ago; apparently well now	0	1
Case	XXVIII. Gonorrhœa 10 times; last attack 4 months ago	1	0

Clinically Cured Cases of Gonorrhœa.

		Positive.	Negative.
Case	XXIX. Gonorrhœa, first attack 2 years ago; impotent 2 years; no evidence of gonorrhœa now	1	0
Case	XXX. Gonorrhœa 4 years ago	1	0
Case	XXXI. Gonorrhœa 3 years ago; had chronic prostatitis; previous test, 4 months ago, positive	0	1
Case	XXXII. Gonorrhœa 2 years ago; had chronic prostatitis	0	1
Case	XXXIII. Gonorrhœa 8 years ago	0	1
Case	XXXIV. Gonorrhœa 2 years ago, lasting 2 months; nothing since	1	0
Case	XXXV. Gonorrhœa—first attack 8 weeks ago; at present no evidence of gonorrhœa	1	0
Case	XXXVI. Gonorrhœa 5 years ago; no signs at present	0	1
Case	XXXVII. Gonorrhœa 6 years ago; does not think he has had a new attack since; treated for chronic prostatitis 2 years ago	0	1
Case	XXXVIII. Gonorrhœa 7 years ago.	0	1
Case	XXXIX. Gonorrhœa, chronic; cocci present 3 months ago; urine clear now	0	1
Case	XL. Gonorrhœa 4 years ago	0	1
Case	XLI. Gonorrhœa 6 months ago; clinically cured now for 6 weeks	0	1
Case	XLII. Gonorrhœa 3 years ago; chronic prostatitis; previous test 5 months ago, positive	0	1
Case	XLIII. Gonorrhœa 5 years ago; cured in about 3 months	0	1
Case	XLIV. Gonorrhœa 3 years ago; has been treated for prostatic and verumontanum trouble	0	1
Case	XLV. Gonorrhœa—previous test, 2 months ago, was positive	0	1
Case	XLVI. Gonorrhœa 4 years ago; had chronic prostatitis	0	1
Case	XLVII. Gonorrhœa 2 years ago; had chronic prostatitis	0	1
Case	XLVIII. Gonorrhœa—first attack 5 years ago; last attack Nov. 17, 1910, abundant gonococci found; local treatment stopped Nov. 28; test made Nov. 29	1	0
Case	XLIX. Gonorrhœa—same case as No. 47, 3 weeks after treatment had ceased; <i>B. proteus</i> , staphylococci, and streptococci found	0	1
Case	L. Gonorrhœa—no acute gonorrhœa in 7 or 8 years; stricture	1	0
Case	LI. Gonorrhœa, question of cure	0	1
Case	LII. Gonorrhœa 5 months ago; many cocci found; irregular in treatment; went on sprees and had several sharp attacks of prostatitis; gonorrhœa apparently cured 3 months after attack, and treatment stopped. Remained apparently cured in spite of heavy drinking for 6 weeks, when test was made; urine was then sent to bacteriologist, who reported urine before prostatic massage contains no gonococci; urine after prostatic massage contains many gonococci	1	0

Joint Cases Treated with Bacterins.

		Positive.	Negative.
Case	I. Gonorrhœa 11 years ago; urine clear now; gonorrhœal rheumatism	1	0
Case	II. Gonorrhœa 18 years ago; stricture for 3 years; gonorrhœal rheumatism for 6 months	1	0
Case	III. Gonorrhœal rheumatism for 3 years	1	0
Case	IV. Gonorrhœal rheumatism for 3 years	1	0

Chronic Gonorrhœa Treated with Bacterins.

		Positive.	Negative.
Case	I. Gonorrhœa 4 years old	1	0
Case	II. Gonorrhœa, duration not stated	1	0
Case	III. Gonorrhœa 5 months; apparently cured	1	0

Joint Cases.

Clinical diagnosis.	Positive.	Negative.	Total.
Gonorrhœal arthritis	13	0	13
Gonorrhœal septicemia and arthritis	1	0	1
Gonorrhœal arthritis (questionable).	4	3	7
Rheumatoid affection of the spine for 3 years; gonorrhœa and prostatitis 7 years ago	0	1	1
Arthritis deformans, etiology unknown, gonorrhœal(?)	1	1	2
Subacute rheumatic arthritis	0	1	1
Acute rheumatic fever	0	4	4
Septic arthritis	0	1	1

Pregnancy.

Cases of pregnancy showing no signs leading to suspicion of gonorrhœa	Positive.	Negative.	Total.
Pregnancy with no signs of gonorrhœa clinically, and gonocœci found only after long search, when positive reaction was reported	14	21	35
Pregnancy with marked antepartum discharge; gonocœci not found	1	0	1
	0	2	2

Women.

On account of the difficulty and uncertainty of diagnosing gonorrhœal infection in women, by means of history or by examination of urethral or cervical smears, it is deemed advisable to tabulate these cases separately.

Clinical Diagnosis.	Positive.	Negative.	Total.
1. Gonorrhœa definitely present or suspected.			
Gonorrhœal cervicitis and urethritis; cocci not found in urethral and cervical smears	2	1	3
Gonorrhœal cervicitis and urethritis; cocci present	2	0	2
Gonorrhœal cervicitis and urethritis; cocci formerly present; now cured	1	1	2
Chronic gonorrhœa	4	0	4
Salpingo-oöphoritis	3	2	5
Gonorrhœal salpingitis	2	0	2
Tender left tube and ovary; diagnosis question between pus tube and cystic ovary	1	0	1
Left ovary enlarged; burning micturition	1	0	1
Left salpingo-oöphoritis; enlarged right ovary; lacerations	0	1	1
Left salpingo-oöphoritis; burning micturition 2 weeks	1	0	1
Postpartum sepsis; gonorrhœal or streptococcic? blood cultures negative; a Gram negative diplococcus found in the uterus	1	0	1
Pyelitis, clinically considered gonorrhœal	1	0	1
Vulvo-vaginal abscess; gonorrhœal	1	0	1
Pelvic peritonitis	1	0	1
Burning micturition for 2 weeks; pus from Skene's glands. No statement of presence of cocci	0	1	1
Fibroid uterus; operation for pelvic abscess and pyosalpinx 5 years ago; supravaginal hysterectomy for right ovarian tumor some years ago; since then pains on the right side	1	0	1
Uterus enlarged; hard, retroverted; tenderness in cul-de-sac; eight miscarriages	1	0	1
2. Miscellaneous cases from the clinic, giving no history or signs of gonorrhœa. Cases of menorrhagia, displacements, tumors, lacerations, abortions, etc.	10	20	30

Summary.

Clinical Diagnosis.	Total No. Cases.	Positive.		Negative.	
		No.	Per cent.	No.	Per cent.
1. Acute gonorrhœal urethritis, first attack.					
(a) Duration 3 days to 3 weeks . . .	5	0	0	5	100
(b) Duration not stated . . .	1	1	100	0	0
2. Acute urethritis; cocci not found . . .	1	0	0	1	100
3. Chronic urethritis of gonorrhœal origin.					
(a) Gonococci present . . .	4	4	100	0	0
(b) Gonococci not found . . .	36	27	80	9	20
(c) No examination made for gonococci, but serum was taken from cases at stage when gonococci are usually absent . . .	8	7	90	1	10
4. Chronic urethritis; history of gonorrhœa doubtful . . .	4	1	25	3	75
5. Chronic prostatitis					
(a) Gonorrhœal history . . .	25	17	68	8	32
(b) Gonorrhœal history doubtful . . .	2	1	50	1	50
6. Sterility, gonorrhœal history . . .	3	1	33	2	66
7. Epididymitis.					
(a) Gonorrhœal history . . .	3	2	66	1	33
(b) Gonorrhœa denied . . .	4	1	25	3	75
8. Verumontanum cases.					
(a) Gonorrhœal history . . .	17	11	64	6	35
(b) Gonorrhœa denied . . .	6	2	66	4	33
9. Miscellaneous cases with no signs or history of gonorrhœa . . .	20	0	0	20	100
10. Gonorrhœa in the male clinically cured . . .	51	22	43	29	57
11. Cases treated with bacteria . . .	7	7	100	0	0
12. Joint affections.					
(a) Gonorrhœal arthritis . . .	14	14	100	0	0
(b) Gonorrhœal arthritis, questionable . . .	7	4	57	3	43
(c) Other joint affection . . .	9	1	11	8	89
13. Pregnancy cases, taken from public maternity hospitals . . .	38	15	39	23	61
14. Gynecological cases.					
(a) Gonorrhœa definitely present or suspected . . .	29	23	79	6	21
(b) Cases with no signs or history of gonorrhœa . . .	30	10	33	20	66

It would seem from the foregoing results that the complement fixation test (using a polyvalent antigen) for gonorrhœal antibodies will have a definite place in the field of clinical pathology as an aid in the differential diagnosis between the various chronic conditions arising from gonorrhœal infection and similar conditions due to other causes. In acute anterior gonorrhœal urethritis we do not get the phenomenon of complement fixation. This is probably due to an insufficient absorption of toxins to stimulate the production of antibodies.

The fact that all cases treated with bacterins give strong positive reactions, would seem to confirm the idea that antibodies specific for the gonococcus are readily formed in the human system.

How far a negative reaction may be relied on (1) to show that a patient is cured, and (2) in cases for diagnosis, to preclude the

possibility of gonorrhœal infection being present, are questions that can only be answered by further study and research.

Next arises the question as to the meaning of a positive reaction and especially as to its meaning in the important group of clinically cured cases of gonorrhœa. Does a positive reaction mean that there still exists a focus of living gonococci somewhere in the body? Or can we assume that the gonorrhœal antibodies may persist for a long time, or even indefinitely, after the gonococci are all dead and the toxins responsible for the production of the antibodies have ceased to be elaborated? We have not many data at hand to aid us in answering these questions, but those which we have would seem to indicate almost conclusively that the first assumption is the correct one, namely, that a positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

Torrey⁹ has shown experimentally that the complement fixatives in the blood of a rabbit immunized to gonococcus, culture A, began to be eliminated ten days after the date of the final inoculation, and continued to be eliminated very rapidly from the tenth to the fiftieth day. From the fiftieth to the seventieth day, when the tests ceased, no further change had taken place. This proves that even in an artificially highly immunized animal the complement fixatives begin to be eliminated very rapidly and in great quantities shortly after the toxins cease to be injected. Immunization of animals against other bacteria, red blood cells, etc., all point the same way. Clinically, also, we have some data at our command. All cases treated with bacterins have given positive results during the period of injections. We have had occasion to examine the blood of several patients four months or more after the injections have been stopped and have obtained uniformly negative results.

Furthermore, we have records of several patients who gave a positive reaction at one stage of the disease and when examined again, after four or five months' careful treatment, resulting in clinical cure of the gonorrhœal infection, have given negative results. We purpose studying the elimination of gonorrhœal antibodies more thoroughly in our future work.

The facts at hand, however, seem to us to prove almost conclusively that a positive reaction is an indication of living gonococci somewhere in the body, and if found in men or women supposedly cured of gonorrhœal infection in the genito-urinary tract, should be construed to mean that they are still capable of infecting others through sexual intercourse. The importance of this in connection with marriage is self-evident.

It is, of course, to be remembered in considering the high percentage of positive results obtained in the clinically cured cases of gonorrhœa, that the great majority of the cases were obtained from

⁹ Jour. Med. Res., 1910, No. 1, p. 95.

a public dispensary. Probably the percentage would be somewhat lower in cases drawn from private practice, where, presumably, the patients are more intelligent and follow instructions and treatment more carefully. The results, however, are highly significant and show that the complement fixation test detects a certain percentage of cases of uncured gonorrhœa, which escaped careful clinical and bacteriological examination.

With regard to operative procedures on the genital tract in women, a positive reaction would in some instances be strongly against the advisability of surgical interference, as it is well known that cases of acute gonorrhœal infection in the pelvis in women do much better if operation is delayed.

In pregnant women, a positive reaction would call special attention to the necessity of prophylactic measures regarding gonorrhœal ophthalmia in her own child, and isolation of both mother and child would lessen the danger of infecting others.

A positive reaction would differentiate between gonorrhœal rheumatism and other forms of rheumatism and arthritis and would indicate the proper line of treatment. To illustrate this we would cite the following case: The patient had arthritis of knee for eighteen years, developing shortly after an attack of gonorrhœa, and was treated for a long time as tuberculous without benefit. The complement fixation test being positive, injections of dead gonococci were given, under which marked improvement took place.

We wish to acknowledge our indebtedness of Dr. James C. Johnston, who suggested this line of work to us. We are deeply indebted to Dr. John Torrey for his great assistance in supplying us with cultures of gonococci used in the preparation of the antigen. Dr. George K. Swinburne has been most courteous in supplying us with abundant clinical material from the very beginning of this study. Dr. E. L. Keyes, Jr., Dr. Charles P. Gray, and Dr. H. C. Bailey have also kindly supplied us with clinical material.

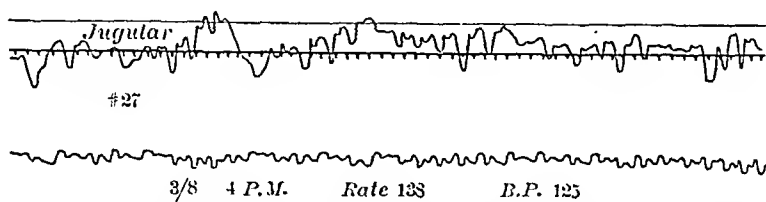
PULSATIONS IN THE PERIPHERAL VEINS.

BY HAROLD C. BAILEY, M.D.,

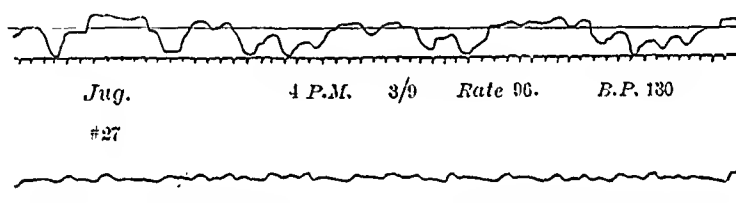
INSTRUCTOR IN PHARMACOLOGY, CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK.

PULSATION is known to occur in peripheral veins in at least three conditions: (1) From the presence of an underlying or contiguous artery; (2) from an aneurysmal varix or direct connection with an artery; and (3) in certain cases of aortic regurgitation in which the impulse is carried through the capillary circulation.

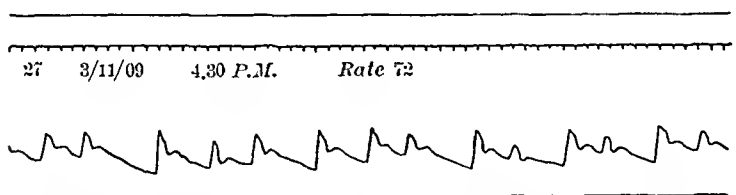
The patient whose case is herewith reported had a pulsation with each beat of the heart in a simple varix or dilatation of the right internal saphenous vein 10 cm. below the internal condyle of the femur. He was a coal heaver, aged forty years, who was first seen in March, 1909. At this time he was suffering from cardiac dilatation, accompanied by the usual symptoms. His legs were very œdematous and no unusual venous dilatations were noticed. He responded exceedingly well to crystalline strophanthin (or ouabain, as it should be called) which he received by intramuscular injection, and he was able to return to his work in a few weeks (Tracings 1, 2, and 3).



TRACING 1.—March 8, 1909; 4 P.M. Jugular (upper) and radial tracings. Pulse very rapid and irregular. Heart in delirium cordis. Jugular tracing shows tricuspid regurgitation.



TRACING 2.—March 9, 1909; 4 P.M. Twenty-four hours later. After crystalline strophanthin.



TRACING 3.—March 11, 1909; 4 P.M. Three days after treatment was started. No murmur or tracing of tricuspid regurgitation could be obtained.

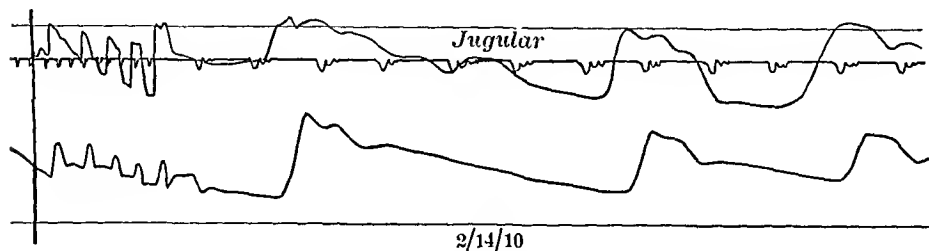
In October, 1909, he entered Dr. Camac's service at the City Hospital¹ suffering again from loss of compensation. He had marked jugular and liver pulsations and the murmur of tricuspid regurgitation. The rhythm of the heart was constantly irregular (Tracings 4 and 5).

When his œdema diminished it was noticed that there was a

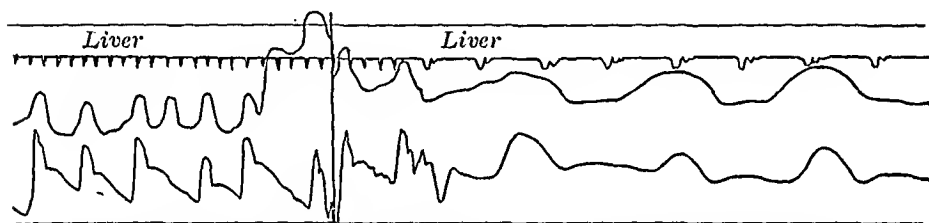
¹ I wish to express my obligation to Dr. Ch. B. Camac for the privilege of reporting this case.

varix 10 em. below the knee in the course of the right internal saphenous vein. On coughing or straining there was a marked enlargement of the varix and a thrill was present as the swelling increased in size.

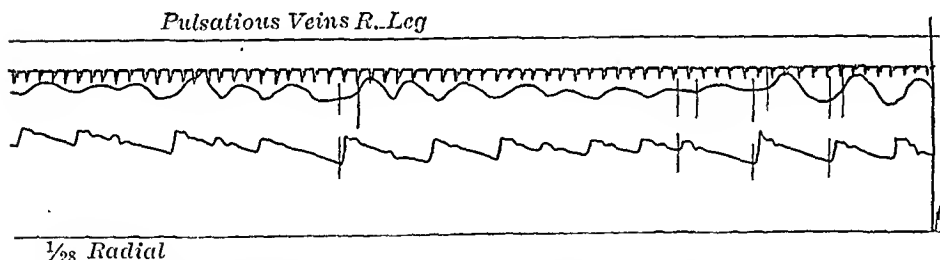
On taking a tracing, it was found that a pulsation occurred in the varix with every beat of the heart (Tracing 6).



TRACING 4.—Jugular tracing (upper) shows the positive wave of tricuspid regurgitation. No auricular wave is present.



TRACING 5.—Upper tracing, liver pulsation, has the same significance as the jugular and its time is ventricular, or about one-tenth of a second before the radial.



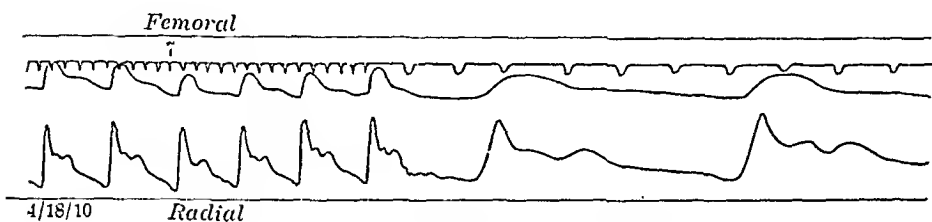
TRACING 6.—Upper tracing from the varix; lower radial. Time marker one-fifth seconds. Arterial time at same location as varix would be one-twentieth seconds after the radial.

Pressure applied above the varix, even as high as the lower end of Scarpa's triangle, which was sufficient to occlude the vein but not an artery, was effective in stopping the pulsations; but pressure below the varix was ineffective.

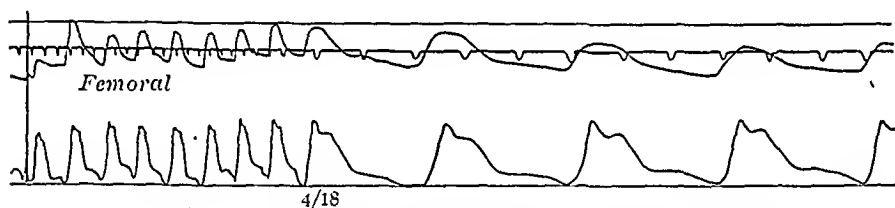
Normal pulsation of the femoral artery at the groin occurs almost exactly at the same time as the radial pulsation, and this is true even in cases of aneurysm of the arch or descending portion of the aorta (Tracings 7 and 8).

The posterior tibial artery as it rounds the ankle beats about one-tenth of a second after the femoral or radial (Tracing 9).

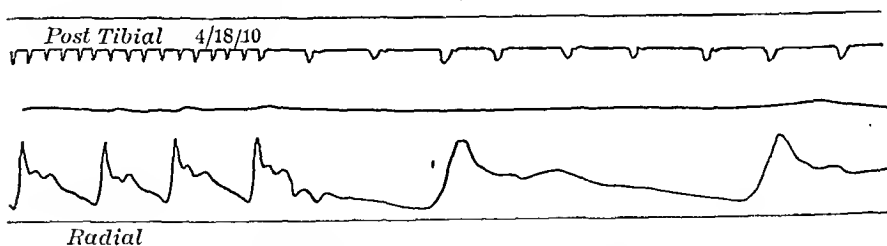
At the location of the varix, which is about midway between the groin and the foot, the arterial pulsation should come about one-twentieth of a second after the radial; but the pulsation that does occur there is from four-twentieths to six-twentieths of a second later. The time reaction varies somewhat, occasionally occurring as early as three-twentieths of a second, sometimes as late as six-twentieths of a second after the radial. This is distinctly in favor of its being a regurgitant wave from the right heart, for such a wave would be moving against the blood current and would be hindered by the more or less opposing valve flaps. Furthermore, contractions that are not of sufficient force to open the aortic valves and pro-



TRACING 7.—Normal femoral and radial time.



TRACING 8.—Femoral and radial time in aneurysm of the arch of the aorta.



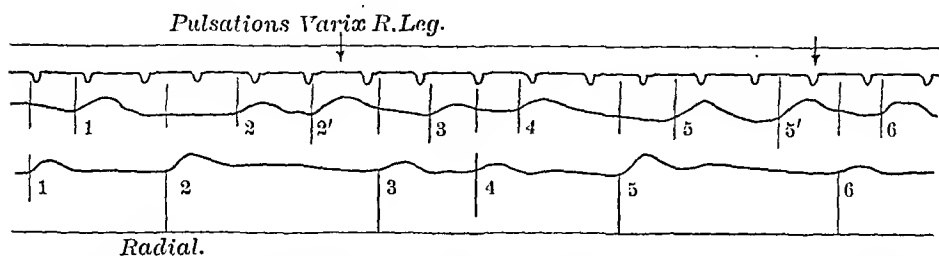
TRACING 9.—Normal radial and post-tibial time.

duce an arterial pulse produce a well-marked wave in the varix (Tracing 10).

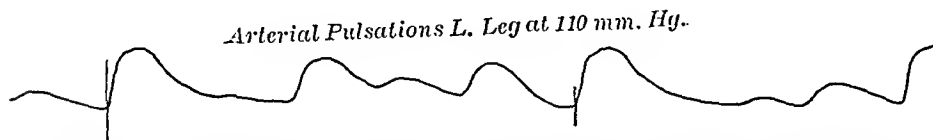
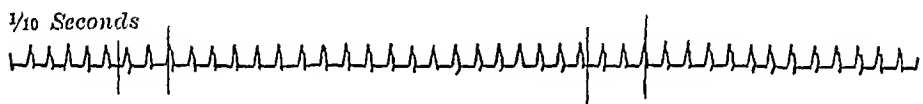
Dr. T. Homer Coffin kindly took a tracing for me with an Erlanger-Hirschfelder instrument. The cuff of the apparatus was placed around the left leg at a location opposite to the varix and an arterial tracing obtained at 110 mm. pressure. This gave an accurate picture of the time relations between the arterial pulsations in the left leg and the pulsations of the varix in the right (Tracing 11).

The time between venous and arterial pulsations at similar locations was two-tenths to three-tenths of a second.

The valves numbering seven to twenty in the internal saphenous vein in the thigh were proved incompetent by two methods. The venous return was stopped by a finger pressed over the vein in



TRACING 10.—Upper tracing from varix below the knee. Lower tracing radial. Time, one-fifth seconds. Notice time relations of the upper venous wave with lower radial and also that waves 2/ and 5/ are produced by contractions which are not of sufficient force in the left heart to open the aortic valves and cause a pulsation in the radial. Pulsation 1 of the varix is two-tenths seconds and 2 is three-tenths seconds after their corresponding radial pulsations.

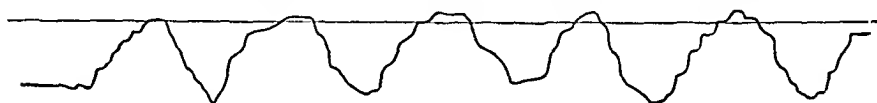


TRACING 11.—Lower tracing. Arterial from left leg just below the knee. Middle tracing. Apex beat—not well defined. Upper tracing. From the varix in right leg. Time marker, one-tenth seconds.

Scarpa's triangle and a few gentle taps were given along the course of the vein just below the finger which was exerting the pressure. These impulses were transmitted to the dilated area below the knee (Schmidt's test). The blood was then drained from the limb and the vein shut off at the saphenous opening. The channel-

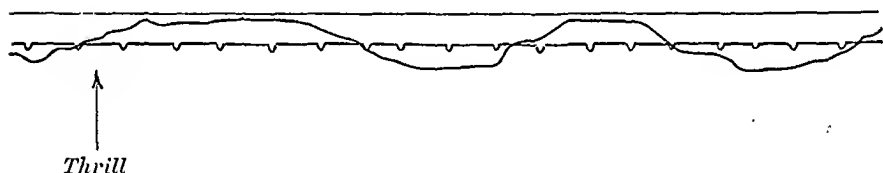
like saphenous vein filled very slowly from below, but when the finger exerting the pressure in the upper part of the thigh was removed the blood flowed rapidly from above filling the varicose area (Trendelenburg's test). While these tests are known by the names given, and have a field of usefulness in diagnosing varicose conditions, they are merely adaptations of the tests of Harvey.

The remaining valve or two in the femoral and those in the external iliac veins were shown to be incompetent by having the patient strain or cough. A thrill was produced in the groin and in the varix and the latter became greatly distended. The fixing and lowering of the diaphragm increased the intra-abdominal tension and temporarily prevented the flow upward. The suddenness with which this occurred sent a venous wave down the leg; and as this wave encountered the flaps of the valves a thrill was produced which could be felt and traced (Tracings 12 and 13).



Each large wave is due to distension of vein during a cough.

TRACING 12.—Large waves due to coughing; small notches on large wave are due to the thrill.



TRACING 13.—Same with fast speed.

The facts that marked tricuspid regurgitation existed with the production of a large wave in the neck and in the liver with each contraction, that the valves of the veins were incompetent, that the time reaction precluded the possibility of an arterial cause, and that pressure above stopped the pulsations while pressure below was ineffective in this regard led to the conclusion that these pulsations occurring in a dilated vein of the leg were produced by the right heart.

In marked contrast to the case just described was that of a patient at Mount Sinai Hospital presenting aortic regurgitation with pulsations of the peripheral veins and whom I was permitted to see through the kindness of Dr. R. Weil. Pulsations were evident in the veins of the back of the hand and the capillary pulse could

be felt anywhere on the limbs. Pressure over a vein stopped the pulsation above. The aortic murmur, though plainly heard, was not loud.

The *étiology* of many cases of varicose veins is obscure, and it seems highly probable that temporary incompetence of the right heart produced by muscular exertion frequently repeated might lead to permanent dilatation of the peripheral veins, and I think this cause was operative in this case.

CONCLUSIONS. 1. The right heart may produce a pulse wave in the veins of the extremities.

2. This pulse wave is considerably later than the arterial pulse.

3. Incompetency of the tricuspid valve may be the cause of varicosities of the veins of the extremities.

With Dr. Camac, I presented this case before the Society of Internal Medicine, February, 1910, and with Dr. Mann before the New York Academy of Medicine, Section on Medicine, in the annual report of the City Hospital, April, 1910.

THE DIAGNOSIS OF PELLAGRA.¹

BY H. F. HARRIS, M.D.,

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It is unfortunately true that practically all of our American literature on pellagra has emanated from sanatoria for the insane. Probably without exception the patients with this malady observed by alienists in these institutions have been subjects who were originally sent to asylums for the mentally defective as a consequence of pellagrous insanity. Hence it follows that the overwhelming bulk of our clinical descriptions of this malady apply to its very last stages, and are of no value whatever in helping us to recognize its earlier manifestations—which is the only period at which we can be of any great service to the unfortunate victim. True, our writers have generally spoken of the disease as observed by them as being “acute,” but they have obviously made the error of confounding the sudden and typical manifestations that occur from time to time in advanced pellagrous persons with the actual beginning of the disease. As a matter of fact, there is no such thing as acute pellagra, it being a malady characterized preëminently by its remarkably chronic nature. As a consequence of the facts just related, the descriptions given by our writers of so-called acute

¹ Read before the Second District Medical Association of Georgia.

pellagra are in no way characteristic of the earlier symptoms, though these occur with great uniformity during the period when the patient begins to show the first effects of maize poisoning. I believe, therefore, that no greater service can be rendered the physicians of the South than calling attention to, and insisting on, the importance of the clinical manifestations uniformly present to a greater or less extent in the earlier stage of this affection—manifestations that have been recognized from the first discovery of the malady and referred to by various writers down to the present time.

The symptoms to which I would particularly direct attention antedate the more obvious manifestations of the malady, such as erythema on the hands and face, denuded tongue, ulcers in the mouth, diarrhoea, and the mental phenomena that we are accustomed to regard as together constituting the symptom complex of this disease. Not only do these earlier symptoms precede the better known manifestations just referred to, but they usually come on years before, in some instances in my own experience being more or less present for twenty years before the patient finally presented the typical characteristics of the disease as usually described. I have no hesitation in going even further than this and asserting that not an inconsiderable proportion of pellagrous individuals never at any time exhibit the characteristic phenomena already referred to, but remain throughout their lives the victims of a mild degree of poisoning which manifests itself in symptoms that have heretofore been regarded by physicians as being of no particular consequence.

Although this disease under the name of "Mal de la Rosa" in Spain and that of "Pellagra" in Italy was unquestionably known to the common people for a considerable period prior to its being taken up by medical men, no mention of it appears to have been made by any writer until 1735, when the affection was described by Caspar Casal. This writer, in the work in which he first discusses the affection in question, made mention of the fact that persons often showed more or less derangement of health previous to the outbreak of the more typical symptoms. At a later time the Italian writers, to whom we owe much of our knowledge of this disease, likewise without exception have insisted upon certain symptoms preceding the outbreak of the more typical clinical phenomena. Frapoli, who was first to recognize this affection in Italy, introduced the term "commencing pellagra" in 1771 for the period of the malady that precedes the classical outbreak, and this writer showed very clearly his appreciation of the fact that there are early symptoms of the disease that differ markedly from those observed at a later time. Four years later Zanetti also indicated quite clearly his recognition of the fact that in pellagra there are minor symptoms that precede the graver manifestations. This writer says, "those in whom the malady is beginning, first complain of a *curious unusual*

lassitude many days, and even many weeks, preceding the eruption, as a consequence of which they carry on with difficulty their agricultural labors." Gheradini, in 1780, again directed attention strongly to the facts already stated, and asserted that this prodromal period has a duration of from twenty to thirty days. A few years later Strombio and Fanzago, both confirmed the observations of the writers already referred to, and strongly insisted that the active outbreak of the classical symptoms was preceded by nervous manifestations and loss of muscular strength. In 1830, Boismont, in summing up these earlier symptoms says "loss of appetite, a disgust for food, a heaviness in the stomach, and dryness of the mouth are the signs that announce the approach of danger." The symptoms already referred to, with many others, which by this time had been observed by various investigators, were accepted by Lussana and Frua in their various papers from 1855 to 1859 as being the earlier clinical manifestations of this disease. They insist on the frequency of pyrosis and of a burning sensation in the stomach. The doctor finds, according to them, "cephalgia, a feeling of heat and heaviness in the head, vertigo, a tendency to melancholy, a general breakdown and muscular feebleness, constipation or diarrhoeal stools almost without odor, red tongue with its surface smooth or covered with numerous villousities, along with furrows running in every direction, oftentimes tremulous, and almost always a little swollen."

Roussel, whose work on pellagra is a classic and still in many particulars the most satisfactory in any language, agrees that there is a commencing period (*pellagra commencante*), in which the symptoms already referred to may occur, although he very properly observes that such phenomena might easily exist as a consequence of some other trifling indisposition, and that we could not regard them as being pathognomonic in isolated cases. He, however, admits, that where pellagra exists endemically, the symptoms might be looked upon as being sufficient to establish a diagnosis, even in the absence of the skin, digestive, and mental symptoms that characterize the malady in its typical form. He also acknowledges that such manifestations may exceptionally persist for a time, and then gradually abate without the more typical symptoms ever occurring. The writer just referred to takes occasion later on in his monumental work on this subject to criticize strongly the view of Strombio that there exists a true pellagra without skin manifestations, which is hardly in keeping with the admission just made. If it be possible for a man exceptionally to exhibit the beginning symptoms of this disease and then return to health without the more typical phenomena that characterize it, he might certainly do the same thing again, and there is no reason why this may not be repeated indefinitely. To this phase of the subject I will return later.

The more recent writers are somewhat disposed to beg the question as to the earlier manifestations, nor is much said concerning *pellagra sine pellagra*, that is, pellagra without skin lesions. Tuczek, in his epoch-making work on the disease ignores this phase of the subject altogether, nor do I find any reference to the matter in the work of Procupui. Vales, of Yucatan, who has written by far the most complete paper on the subject emanating from an American, admits that now and then the disease may occur without the skin symptoms. He says: "the most important anomaly seen in this disease are those remarkable cases which Strombio calls "*pellagra sine pellagra*;" in this case the disease shows clearly all of the typical symptoms of the nervous system and the intestinal tract, notwithstanding that no erythema occurs." In the still more recent work of Marie I have been unable to find any allusion to this most important matter.

From the foregoing it is seen that among students of this disease it is generally accepted as true that there are preceding the outbreak of the typical symptoms minor and less characteristic phenomena. However, they are by no means a unit as to the occurrence of Strombio's "*pellagra without pellagra*," and it is to this most important matter that I wish now particularly to direct your attention.

While no one is less disposed to trust to *a priori* reasoning than myself, it seems to me that this is one of the instances, if we accept the common view as to the etiology of the malady, in which we may safely deduct from analogy certain probabilities that bear with great force on this particular question. It is certainly true if pellagra be caused from fermented maize that the malady is due to the presence of certain toxins that are formed in this cereal, and not to living bacteria. Such substances being chemical entities and probably of an alkaloidal nature, their action on the body might be justly compared to the effects produced on the human organisms by similar poisons, with the properties of which we are well acquainted. For example, it is well known that a man might be given indefinitely very small doses of strychnine without producing any obvious effect. With somewhat larger amounts we would begin to observe what we call the *physiologic* action of the drug, and this might again be continued for considerable periods of time without producing untoward results. If still larger quantities be administered we then begin to see the poisonous effects, the patient ultimately dying if this be kept up from the typical symptoms that characterize the toxic action of this drug. So, also, might we employ for our experiment the alkaloid of belladonna, another substance like strychnine, that acts upon the central nervous system. Very minute doses of atropine would produce no obvious results. Still larger ones would occasion the well-known symptoms that characterize the physiologic effect of the medicament, while very large amounts of this alkaloid would produce immediate

death. It is said that if this drug be given in very moderate doses for a long period of time that it impairs the health, destroys ultimately the mental faculties and in the end produces death. It is asserted that the poison employed by Lucrezia Borgia was a compound, the principal ingredient of which was an extract of belladonna, and it is generally said that her victims died with the symptoms just referred to. The action of atropine, particularly, may be compared to that of the toxins that produce pellagra, since in both instances alienation and death are the consequence of the taking for a long time small doses, and both evidently act primarily on the nervous system.

Presuming then, as we do, that the view is correct that pellagra is caused by ptomaines from corn, it could hardly be otherwise than that in small doses we would have no appreciable effect, but that in larger amounts the patient would suffer a certain deterioration of health, while in still greater quantities the full toxic action of these substances would be produced, and the patient would be saved from a very quick death, only by becoming too ill to eat further of the food containing the poison.

Assuming the conclusions just arrived at to be true, we should be able to discover symptoms, however slight, in those who are being poisoned with small doses of the substance or substances in question, and the earlier stages of the malady should, therefore, have a definite symptomatology. But we should not overlook the well-known fact, that different persons vary greatly in their capacity to resist disease-producing agencies. It may be confidently asserted that one individual would show decided ill-effects from a given dose of these toxins, while another would remain perfectly normal. We have also to consider the matter of acquired immunity, there being no reason to doubt that the continuous taking of these poisons in small doses would result in the production of a certain degree of tolerance in most, if not all persons. The view just expressed, however, cannot be stated as absolutely true; there are other facts that might be looked upon as pointing in the opposite direction, since it seems true that those who have once suffered from a pronounced form of pellagra are exceedingly susceptible thereafter to even a slight degree of poisoning from the toxins concerned.

Theoretically, then, it would seem highly probable that we should have symptoms of slight poisoning in persons taking only a small amount of the toxic agents, and I am perfectly confident that closer study will demonstrate beyond question the correctness of Strombio's view that one may have pellagra without skin lesions. I have no hesitation in going still further and saying that the patient, year after year, may suffer from a fairly well-defined series of disturbances without there being an erythema, mental symptoms, or ulcerative changes in any part of the gastro-intestinal tract. I believe that these same patients, if given a sufficient quantity of poison,

would probably, in all instances, develop the more pronounced symptoms, and I have actually seen an instance where the patient had suffered for twenty years before any of the more severe phenomena appeared.

In the foregoing it has been assumed, as we appear to have every right to do, that pellagra is not produced by a living virus, but it might be well to inquire if the clinical picture of the malady would likely be different if our conclusions were incorrect. In reply it might confidently be asserted that there would be in all probability in this case a *progressive* clinical picture, with well-defined stages, until the final termination in recovery or death. There is no reason for believing, nor is there analogy for assuming, that if it were an infectious process the malady would for years appear at certain seasons with intervening periods of practically perfect health.

Beginning Symptoms. The symptoms that indicate the earlier stages of pellagra are partially of a temporary character, lasting a few weeks or a month or so, to be followed in the beginning by an almost complete return to health. In addition to these there are others that, in the course of time, slowly come on and ultimately become chronic.

These patients, pretty uniformly, give a history of being well in the winter, particularly in the earlier stages of the disease, and of having something in the nature of what are commonly called "bilious" attacks in the spring, summer, and autumn. The tongue is furred, there is more or less obvious indigestion with intestinal putrefaction, a feeling of malaise, and considerable mental and physical depression. These attacks recur from time to time, and gradually the patient reaches a stage, during which there is more or less constant indigestion, especially in the spring, summer, and autumn. There is frequently a burning sensation and a feeling of heaviness in the region of the stomach, accompanied by pyrosis in many instances. There is usually fermentation of the food in the intestines as indicated by considerable quantities of flatus.

More Advanced Symptoms. After this has gone on for a number of years the patient begins to exhibit in the spring still more pronounced disturbances. He becomes unaccountably and curiously weak with no disposition to engage in any physical labor. The mind is also pronouncedly affected, the patient viewing life in a most gloomy manner, and he ceases to care for those things that previously interested him most. He often has more or less vertigo. As time goes on the patient complains of disorders of sensation, particularly a curious burning, which is now not confined to the stomach but frequently occurs in other parts of the body, notably in the feet and legs. I have been unable to persuade myself as to whether these patients really have disorders of the cutaneous nerves of touch, pain, and of heat and cold, though it is theoretically highly probable that

this is often the case. They do not appear to have disturbances of the muscle sense—none of those coming under my observation being ataxia. Many patients complain of pains in the abdomen and back; vomiting is not infrequent. The reflexes now show marked exaggeration in the majority of instances—less frequently they may be diminished, and in occasional cases no change will be found. I do not believe it to be possible always to recognize this malady merely from the manifestations referred to in the description of the earlier stages of the disease, but when they are combined with those later mentioned I think a clinician would be justifiable in making a diagnosis of pellagra. The history of bad health in the spring, summer, and autumn, repeated for a number of years, followed by a curious and unaccountable loss of physical strength and mental vigor, a gloomy outlook on life, burning sensation in the stomach, legs or feet, digestive disturbances and a change in the reflexes constitute a clinical condition that, so far as I am aware, could be ascribed to no other cause. If, however, we are in doubt, the matter is of sufficient gravity to justify us in advising the patient to take the precautions that one would naturally suggest if the fact of the diagnosis were beyond question.

I have seen many cases of this kind, all of whom without exception have immediately improved as soon as they were directed to leave off all corn products, and who were given good food, rest in bed, and arsenic. The reflexes of such patients still remain abnormal, and to none of them has their former strength returned, but they are better in every other way, and I believe if they persist in taking the proper precautions they will have no return of the disease. It is, of course, all but certain that such patients have organic lesions in their cords, and that many of the parenchymatous cells of the central nervous system have been destroyed, and it is, therefore, highly improbable that they will ever regain their muscular strength completely, or that the reflexes will return again to the normal.

Below I give the history of three of these cases:

CASE I.—Mrs. S., aged forty-six years, a native of Georgia, was first seen on January 4, 1909. The family history was negative. Patient had typhoid at nineteen years of age. No other trouble of serious character. In recent years has not been a good sleeper. Was very energetic up to the beginning of the recent illness. Is a good eater. Eats some sweets and fruits daily; also hot breads, often with melted butter, potatoes, some so-called breakfast foods, soups, tomatoes, condiments, and corn products daily. Eats little meat. Coffee once daily; tea rarely. In the spring of 1903 the patient's trouble began with great weakness and some indigestion. In September she began to improve and by November was entirely well again. The following spring the weakness recurred, accompanied by indigestion and a good deal of pain in the abdomen. There

was considerable mucus in the stools and later in the summer the patient had diarrhoea for about a month. Since this time the patient has been constipated, but there are frequently more or less pains in the abdomen. This condition has persisted to the present time, the patient being extraordinarily weak and gloomy. Upon physical examination the following notes were made:

The body is thin and rather pale; tongue is raw at the edges and sores at the inside of the lips. Teeth are fair; pulse, 66; respiration, 18; temperature, 98. Right kidney is somewhat lower than normal. Slight tenderness in left inguinal region. Reflexes much exaggerated; sole reflexes absent. Feces normal. Urine, 690 c.c. in twenty-four hours; reaction acid; specific gravity, 1015; no sugar; trace albumin; urea, 16.32 gm.; phosphates, 6.63 gm.; chlorides, 11.48 gm.; microscope shows a few pus cells, but no casts. Under rest and arsenic, with abstinence from corn products, patient is now practically well.

CASE II.—Mrs. A., aged fifty-four years, a native of Georgia, was first seen April 25, 1909; family history negative. Patient had jaundice in 1901, from which she did not recover in about a year. Bilious attacks rather frequent. In 1904 had some sort of skin eruption on the hands. Patient cannot describe it sufficiently accurately to give one an idea as to its probable nature. Now and then pimples come on back of the legs and form small scabs. Recently the patient has had insomnia; sleeps about seven hours. Was very energetic before present trouble began. Was moderate eater; eats fruits, sweets, hot breads with butter and gravy, potatoes, so-called breakfast foods, and corn products daily. Patient eats little meat. Chews well. No coffee or tea. For many years patient has been gradually growing weaker, and now feels a complete indisposition toward all physical and mental exertion. She is gloomy and has lost memory more or less. Complains that she cannot think. About two months ago she had a feeling as if a band were gripping the left arm, and this sensation extended to the whole left side of the body. Not infrequently she has jerking of the muscles of the left side. At times has intense back-aches, and has recently had something like rheumatism in her fingers. Appetite poor. She has lost much flesh. Bowels irregular.

Physical Examination: Patient appears fairly well nourished, but is pale. Tongue is coated; teeth have all been extracted. Pulse, 86; respiration, 18; temperature, 98.4. Hemoglobin, 90. No examination was made of the cells. All of the patient's organs appear to be normal. The deep reflexes are greatly exaggerated, especially on the left side. Feces, negative. Urine, 1375 c.c. in twenty-four hours, acid, specific gravity 1004; no albumin or sugar; urea, 11.60 gm.; phosphates, 2.75 gm.; chlorides, 12.55 gm. Moderate amount of skatol and indican; Ehrlich's reaction moderate; microscope shows nothing unusual.

CASE III.—Mrs. G., aged forty-five years, a housewife, was seen in consultation with Dr. Wesley Taylor, on September 12, 1909. It so happened that I had been called in to see this patient twenty years before, and remember distinctly that she was suffering from a condition, that I at that time, considered gouty. During the summer of 1889, she had been in ill health with considerable indigestion, and had been confined to her bed on account of general weakness for some time previous to my having been called in. As to whether or not she had the other manifestations common in early pellagra I cannot, at this time, recall, but the symptoms as above given were present. Her husband informed me that she has suffered in the same way, more or less ever since, in the summer. The patient was first seen by Dr. Taylor on August 18, 1909. On April 1, 1909, the patient, while out shopping, was seized with nausea accompanied by pain in the limbs, abdomen, and back, continuing from the early morning until noon, when she was relieved as suddenly as the symptoms came on. Some time after this she was operated on for hemorrhoids, these having been evidently produced by constipation. She continued, during the summer, to suffer from pains in the back and limbs, and also from nausea, getting better and then worse. The patient has passed a considerable amount of mucus from the bowels recently. Does not sleep well, is wakeful, and dreams much. Is as tired in the morning as when she went to bed at night. Considerable pain in the back of the neck and in the stomach; also has much dizziness, and hot flashes up and down the back. Patient has indigestion, from which she has suffered for many years. Has been curiously and unaccountably depressed all the summer. All the organs appeared normal on examination. The deep reflexes were greatly exaggerated. The temperature, pulse, and respiration remained normal until the patient had been in the hospital about four weeks. After this there began to be periods of slight fever with some quickening of the pulse and respiration, to be followed by a return to the normal. At the end of another week the pulse, respiration and temperature would remain throughout the twenty-four hours above the normal, and later continued to go up until on the day of death, which was on October 1, the temperature was 107; respiration, 54; pulse, 158. Simultaneously with the febrile movement there began to appear short flurries of diarrhoea, to be followed by a normal condition of the bowels for a day or so, with return again to undue frequency. The patient's bowels did not move during the last twenty-four hours of life, but in the days preceding, there were several movements daily; from the middle of September to the middle of October the feces contained a considerable amount of mucus. During the entire period of observation the patient complained a great deal of pains in the limbs and in the back, often of nausea, and constantly of being utterly worn out. The week after she was first

seen by me, she developed sore mouth, followed by ulceration, and likewise an inflammatory condition of the throat, all of which grew worse until her death. About the same time it began to be quite obvious that her mind was not normal, and she continued to show most decided evidences of alienation, which gradually grew worse to the end. It is particularly of interest to note that at no time did she ever show a skin eruption. We have, then, here a case where the patient had been ill for at least twenty years with symptoms that might be regarded as pellagrous, later followed by a great and inexplicable weakness, pains in the limbs and back, indigestion, exaggerated reflexes, and, lastly, by diarrhoea, sore mouth and throat, and loss of mentality, without skin eruption at any time. If this be not a case of *pellagra sine pellagra*, I am at a loss what to call it.

VACCINE THERAPY AND A SIMPLIFIED OPSONIC INDEX.

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VACCINATION began with Jenner and culminated with Wright. The therapeutic principle is the same whether we use a live attenuated virus or a dead unattenuated virus. In either case the purpose is to cause the production of specific antibodies in the blood. Such is the relation of the smallpox vaccine to the opsonic vaccine.

But, while the smallpox vaccine was a purely empirical discovery, the opsonic vaccine is as purely the product of scientific methods—of purposeful experiments and deductions from the accumulated data of preceding investigators. In the beginning, vaccination for smallpox was made with a virus of unknown composition, uncertain purity, and unmeasured dose. But the opsonic vaccine from the beginning was of known composition, of certain purity, and of measured dose. After smallpox vaccinations, nothing was known of what took place within the body excepting the symptoms of the patient and the progress of the sore on the skin. After opsonic vaccination, the opsonic power of the blood serum and the phagocytic power of the leukocytes may be measured and stated as definite indices.

In vaccination for smallpox we induce immunity by the production of disease. In opsonic vaccination we are enabled to induce immunity without the production of disease. Therefore, following smallpox vaccination we have a symptomatology, both local and systemic, sufficient for medical supervision. But, following opsonic injections, we have no symptomatology either local or systemic depending upon the incubation, growth, distribution,

and toxicity of a living virus within the body. Instead, we have purely a reaction in the blood and tissues to the chemical substance of the bacterial cell.

This reaction in many cases may be accompanied by redness, swelling, and pain about the site of injection, and by chills, headache, *backache*, nausea, *malaise*, and fever. But in some cases the reaction may be profound without a symptom local or systemic. In any event, after the subsidence of symptoms or after a reaction without symptoms we must be guided to the size and time of the next injection by the opsonic index—or by guesswork.

After an opsonic injection the patient may improve, grow worse, or remain unchanged. If the patient improves after each injection until cured, we may say that guesswork more or less acute and more or less aided by experience has been successful. But if the patient, after any injection, remains unimproved or grows worse, there is no guesswork, however acute or experienced, that can determine whether the dose was too small to arouse a reaction or so large as to induce a negative phase from which recovery may be doubtful. Even in the first supposition, where improvement and cure result, we may nevertheless state that laboratory control would have made a yet more satisfactory case; because we thus could have determined the best time and dose for each injection, rather than have relied upon a loose approximation which the patient's superior powers of reaction prevented from resulting in failure.

There is, however, a strong and increasing tendency on the part of the profession to rely upon the indefinite clinical rather than upon the definite laboratory control. An examination of the advertising sheets of our journals, as well as of the articles, and attention to the discussions at society meetings, as well as to the reading of papers, furnishes us with some explanations of this anomaly. The estimation of the opsonic index as devised and practiced by Wright and his followers is a complicated, delicate and time-consuming procedure. It is no longer true that physicians have neither the laboratory facilities nor the training to make these estimations. But, on account of the delicacy of the process, even special laboratory workers are liable to wide errors. The method, therefore, so beautiful and conclusive as a means of investigation into the problems of immunity, becomes often misleading and always expensive as a mode of daily practice. At the same time, through the medium of advertisements, we learn that great pharmaceutical houses, with splendid laboratories and trained workers, are furnishing bacterial vaccines in permanent and convenient packages, with directions for use, without the bother or expense of estimating the opsonic index. Many able practitioners have already committed themselves in papers and discussions to the use of such vaccines or to the use of autogenous vaccines, guided by clinical symptoms alone, and will perhaps continue to defend such practice on the ground that the

opsonic index in general has proved fallacious, and that thus only can vaccines be brought into general use for the benefit of humanity.

If vaccine therapy is of such value, if the opsonic index is so fallacious, and if, also, the clinical symptoms are insufficient guides to the size and frequency of the bacterial dose, then we have the option of improving the clinical picture or improving the opsonic index. The clinical picture must be left to nature, but the opsonic index, with its promise of precision instead of empiricism, remains with us.

GENERAL OBJECTIONS TO THE OPSONIC INDEX. What are the objections to the opsonic index? As a method of investigation, in the hands of Wright, there is no objection. Wright's work will forever stand as the foundation of opsonic therapy. However, it has been urged that opsonins are only one class of protective substances in the blood serum and that the opsonic index gives us but a single factor of the many which enter into an immunity. It also has been stated that patients with lowered opsonic indices have nevertheless improved clinically and that patients with high indices have progressively failed and died in the face of laboratory evidence of improvement. Can these statements be true and yet the opsonic index be of value?

These objections bring us at a bound into one of the most complicated problems of pathology—the composition of the blood plasma. Blood is like coal-tar; it contains an infinity of substances. The food supply, the waste and sewage of tissue, internal secretions yet unnumbered and specific antibodies for almost any foreign substance—this heterogeneous array lay unsuspected for centuries in the apparently simple homogeneous straw-colored serum of the blood. Doubtless after generations of medical workers for the common good have passed away, physiological chemists will still continue to isolate and catalogue specific substances in human blood.

At the present time we speak of antitoxins, agglutinins, lysins, precipitins, opsonins, albumin-splitting ferments, and in general of bactericidal powers of serum. We recognize that nature does not rely upon a single type of defense for all bacterial invaders. But it is nevertheless plain that the body defence in the presence of bacterial invaders consists of two distinct efforts—first, for the production of an antidote for the bacterial poison; and, second, the disposal of the living or dead bacterial cell. The first is the production of an antitoxin or a precipitin; the second is accomplished by several means, such as, (*a*) the formation about the invaders of a wall which may become calcified or which may remain inflammatory with resulting abscess and ultimate drainage; (*b*) the disintegration of the bacterial cell by lysins, agglutinins, or albumin-splitting ferments; and (*c*) the ingestion and digestion of bacterial cells by the leukocytes.

These processes contribute one to the other. The disintegration of the cell body throws into solution the cell toxins which must be taken care of by the antitoxins or precipitins, and the fierce phagocytic zeal of the leukocytes causes them to crowd about the bacteria in such numbers as to form both the inflammatory wall and the pus within.

It is clear that the opsonic and phagocytic indices tell us nothing about antitoxin or precipitin, but it is no less clear that they do tell us about any substance which in any degree injures the bacterial cell. Wright's work, amply confirmed, has demonstrated that the power of the leukocyte to ingest and destroy bacteria is increased or diminished by the presence of substances in the serum which act, not upon the leukocytes, but upon the bacteria. The general term opsonin, therefore, does not necessarily designate new substances in the serum, but would include under one term all those substances which, acting upon bacteria in the blood, render them a more easy prey to the warrior leukocytes.

Therefore, when we estimate the opsonic index we estimate the power of the blood to destroy the bacterial cell by phagocytosis, and excepting in the case of lysins powerful enough to dissolve and thus destroy unaided the bacterial cell, we may affirm that in those diseases where bacterial therapy is successfully employed phagocytosis is nature's method for removing the bodies of bacteria from the system. The opsonic index, therefore, is not in principle fallacious.

Concerning the statement that patients with lowered indices have improved clinically, we may infer that toxins were causing the symptoms and that the production of antitoxins by the body resulted in improvement in spite of lowered phagocytosis. Nevertheless, true recovery cannot be said to result unless phagocytosis be finally sufficient to rid the body of the bacterial intruders. The chronic "typhoid carrier" is an example in point.

Similarly, concerning the patient who dies although the index has risen, we may infer that certain tissues or organs have been overcome by toxins before the increased phagocytosis could remove the cause or before antitoxins could be elaborated. If nerve tissue and heart muscle have been sufficiently poisoned by bacterial products, the complete neutralization of the toxins by antitoxins or the complete eradication of the bacteria by phagocytosis will not avail to save life.

These facts do not in any way deprive the opsonic index of its value, which is to inform us of the rise and fall in the blood of the power to destroy the bacterial cell. We are thus enabled to give the vaccine injection in the decline of the positive phase and to withhold the dose or give a minimum during a negative phase. We also may be informed when the defensive processes are at their height and when our duty is simply to watch the case and await the physiological moment.

To re-state the foregoing conclusions in clinical terms we may say that after an injection of a vaccine composed of non-living bacterial substance, we obtain in the patient reactions of two kinds. One reaction is to the chemical poison or toxin of the bacterial substance and results in the production of antitoxins. The other reaction is to the physical body of the bacterial cell and results in the production of opsonins and an increased phagocytosis. While both reactions depend upon cellular elements soluble in serum, yet opsonins are excited by elements not necessarily toxic. The first reaction is measured by clinical observations; the second reaction may be measured by the opsonic index.

MODIFIED VACCINES. We may venture further, and state that by the injection of the soluble poisons produced by bacterial growth but without the substance of the bacterial cell, we may produce an antitoxin reaction without the production of opsonins. Conversely, a vaccine may be prepared which will produce an opsonic reaction without the production of antitoxins. This fact, I believe, may be shown by the use of split products of the colon germ-substance furnished me by Dr. Victor C. Vaughan, of Michigan University.

Vaughan showed that any proteid body—bacterial substance as well as egg-white—could be split into two bodies, *in vitro*, one of which was a poison and the other a non-poison. The injection of the poisonous half would necessarily give rise to a specific antitoxin or precipitin, but the injection of the non-poisonous half gave rise to the production of a proteid splitting ferment or lysin in the blood which “sensitized” the patient to the colon germ; that is to say, colon substance introduced into the circulation after such sensitization would be rapidly split up by a process indistinguishable from a bacteriolysis.

By using the non-poisonous sensitizing portion of the colon substance, in a case of colon infection of the urinary tract, I found that the opsonic index was regularly increased, and increased without the production of negative phases. Yet, after the injection there were no clinical symptoms whatever—nothing at the site of injection and nothing systemic.

It would seem from these observations that proteid splitting ferments or lysins act as opsonins. Further work may show that what seems true of the colon substance may be true of other bacterial substances and that the use of the sensitizing portion of the bacterial cell will increase the safety and precision of vaccine therapy. There is one difficulty, however, in the use of split products. This is the necessity of using a stock instead of an autogenous culture.

RELATION OF OPSONINS TO BACTERIOLYSIS. After the colon opsonic index had arisen to a certain grade, colon bacilli could no longer be found on the stained slides. Repeated attempts demonstrated that the bacilliary emulsion, when mixed with the blood

of a properly treated patient and incubated for fifteen minutes, underwent bacteriolysis. The colon bacillus was the antigen, and the fresh blood contained both complement and antibody (anticolon amboceptor). The process is in consonance with the Wassermann reaction and Ehrlich's side-chain theory.

If opsonins and bacteriolysins are separate bodies, then two separate lines of immunity for the same germ may develop simultaneously. But opsonins are not proved to be separate bodies, distinct from all other immunizing substances. Apparently in the case of colon infections an opsonic immunity may pass into an immunity by lysis. Apparently an increased opsonic index, with increased phagocytosis, represents a stage of incomplete bacteriolysis. As complete bacteriolysis is approximated, the number of germs found without and within the leukocytes will rapidly diminish and the opsonic index will fall. Finally, when bacteriolysis is complete within the fifteen minute interval allowed in opsonic work, the opsonic index would stand at zero. But the index of immunity would have arisen to its theoretical limit. The fact that no germs can then be demonstrated within leukocytes indicates that the union between antigen, amboceptor, and complement took place before phagocytosis were accomplished and that bacteriolysis, in the case of those germs ingested, would then continue within the body of the leukocyte.

Therefore the estimation of the opsonic index and the detection of a bacteriolysis should be brought within the same report. Fortunately the opsonic procedure is singularly adapted to the detection of bacteriolysis. It is required merely to observe the condition of the bacteria on the stained slide prepared for opsonic counting. Agglutination instead of bacteriolysis may take place, but the opsonic method herein described prevents bacterial clumping. We must recognize in these higher levels of immunity the limitations of opsonic and phagocytic indices.

INDIRECT AUTOGENOUS VACCINATIONS. The injection of bacteria or their products is not the only way of bringing about inoculation and immunity. Massage, Swedish movements, Bier's hyperemia, the surgeon's knife, and the x -rays may, upon occasion, bring about the liberation and absorption of various disease products, which are of necessity autogenous. The proper use of the x -rays¹ in tuberculous glands of the neck and in lupus, has been shown to increase the opsonic index for the tubercle bacillus. Similarly, in cases of *Staphylococcus acne*, the index for that particular germ is increased by x -ray applications. The effect is specific. The general opsonic powers of blood are not altered. The reaction

¹ See Specific Immunity and X-ray Therapeutics, by A. W. Crane, AMER. JOUR. MED. SCI., 1908, cxxxv, 421.

is found to be directed against the morbid agent within the area x-rayed, and no other.

The advantage of the x-rays lies in the fact that the immunizing substances set free are always autogenous and that it may be used where the disease-producing agent is not bacterial and is as yet unknown.

TECHNICAL OBJECTIONS TO THE OPSONIC INDEX. While defending the principle of the opsonic index, I would advance the following objections to the orthodox opsonic technique:²

1. *The time necessary to estimate an opsonic index makes it an impossible procedure in private practice.*

2. *Too much blood is required from patients and controls.*

3. *A pool of twenty normal sera is unqualifiedly impossible to obtain in private practice.* It is usually impossible to get even two or three sera for controls, excepting from one's own family, and these may not represent the normal. Furthermore, reliance on a pool may lead to serious errors, because any little infection may greatly alter the index of anyone, so that, strictly considered, each serum of the pool should be separately tested, which emphasizes the impracticability of the pool.

4. *The power of the leukocyte varies in different individuals.* This has been proved by Potter and confirmed by us by testing the leukocytes from different individuals to the same serum. This makes a control by pool necessary in every case tested by Wright's method.

5. *Many leukocytes are destroyed by washing and centrifugating, so that the proportions are altered.* Leukocytic fragments are very commonly met with on opsonic slides and lead to counting errors of unknown proportions.

² Wright's Method of Estimating the Opsonic Index. The blood to be tested is drawn from a skin puncture into special bent pipettes. The serum is separated by hanging these pipettes on the arm of a centrifuge and rotating. Specimens of blood from twenty healthy people (if possible) are similarly treated to obtain sera which are mixed to form the control serum, or "pool."

The leukocytes are obtained by allowing 15 or 20 drops of blood from a healthy person to fall into a centrifugal tube holding 15 c.c. of an aqueous solution of sodium chloride, 0.85 per cent., and sodium citrate 1 per cent. This is a wash solution which prevents clotting. The blood is gently mixed with this solution and centrifugated with care until the corpuscles are packed in the bottom of the tube. The supernatant wash solution is then decanted or siphoned off, and the corpuscles mixed with an 0.85 per cent. sodium chloride solution and again centrifugated. A third washing is thus given to remove the serum completely.

The top layer of the packed corpuscles (leukocytic cream), rich in leukocytes, is drawn into a pipette and removed for use. A standardized suspension of the bacteria in question should be at hand. One volume of serum to be tested is mixed with one volume of washed corpuscles and one volume of isotonic bacterial suspension. This mixture is taken up by a capillary tube which is placed horizontally in a suitable thermostat, where it is kept at 38° C. for fifteen minutes. The mixture is then blown out on slides, spread, dried, fixed, stained, and counted.

The pool or control serum is then put through exactly the same procedure and the resulting slides stained and counted.

The average number of bacteria found per leukocyte in the serum of the patient is divided by the number of bacteria per leukocyte in the pool serum. The resulting figure is the orthodox opsonic index.

6. *Leukocytes suffer injury from trauma, cold and contact with wash solutions in the process of centrifugal washing.* The idea is commonly conveyed, in papers on opsonic work, that the leukocyte is a constant and has nothing to do in the process of phagocytosis excepting to register the quantity or quality of opsonins in the serum. I have been deeply interested in watching the leukocytes in the midst of bacterial suspensions on a warm stage under the microscope, in order to observe the process of phagocytosis. The leukocyte is here seen to be an active, not a passive, agent. As germs float near, a slender finger or fingers reach out to enclose them. Or, again, germs may lie in contact with the cell wall and not be taken in. The leukocyte seems to exercise an individual selection and takes in bacteria by voluntary effort only. On dried and stained slides these pseudopodia may be seen in plenty where a stain is used, such as Ehrlich's tri-acid stain, which defines the cell body. In this way many a germ will be counted as lying within the cell which would be missed if the long protoplasmic finger were not made visible. This action cannot be due to the surface tension effects observed in artificial amoebæ, because it varies for the same leukocytes in different sera and for different leukocytes in the same serum. The leukocyte is a living unicellular animal whose health and vigor is to be reckoned with hardly less than are the properties of the serum.

EXPERIMENTS IN SIMPLIFICATION. Many difficulties in Wright's methods arise from the processes necessary to separate serum from corpuscles, and the white cells from the reds. Inasmuch as serum and washed corpuscles are re-combined in the same proportions approximately in which they exist in the untouched blood, the query arises: Why not use the whole blood? We find that Wright, Leishman, and others tried the whole blood and rejected it because of clotting. A second query arises: Why not, then, use sodium oxalate or citrate or leach extraet and prevent clotting? We found, however, that the use of any of these substances was attended by two objections: (1) The white cells agglutinated to a greater or less extent. (2) The phagocytic or opsonic power was markedly altered.

We thought that if we could overcome the first, possibly the second would prove to be a constant factor of calculable extent. Simple dilution was first tried. To accomplish this, an ordinary leukocyte pipette was used, giving a dilution of one volume of blood with nine volumes of the germ suspension (in sodium ehloride, 0.85 per cent.; sodium citrate, 1.00 per cent.; water, 100 per cent.). This was an improvement; plenty of separate phagocytes could be found, but some clumping of the leukocytes still occurred.

The obvious manœuvre was to make use of the mixer or glass bead within the bulb of the pipette. To do this I filled a bowl with water at 38° C., or body heat, and rotated the submerged pipette

slowly between my fingers. A slight movement was thus imparted to the corpuscles and the agglutination of leukocytes no longer occurred.

The next step was to obtain the factor of phagocytic interference due to the citrate or oxalate. We approached this problem by seeking to reduce the factor of interference to its lowest terms. This is to say, we progressively lessened the per cent. of citrate or oxalate in the diluting fluid so as to determine the smallest quantity actually necessary to prevent clotting of the blood when rotated in the mixing pipette. To make a short story shorter, we found that so long as the pipette was rotated no citrate or oxalate was required to prevent clotting; that a dilution simply with normal salt solution fulfilled requirements. Our problem, therefore, of estimating the factor of phagocytic interference due to clot-preventing substances vanished, because normal salt solution has no factor of phagocytic interference.

The blood is thus received into a neutral isotonic saline solution, so that the plasma is, in effect, the "salted plasma" of the physiologist. Clotting is delayed, not prevented.

It was a matter of simple experiment to reduce the factor of rotation to its lowest terms; that is, to ascertain how little motion serves to prevent clotting. To this end I removed the works of a common cheap clock and by slight alterations obtained a device by which the pipette could be rotated slowly at a constant rate. We found that the practicable speed, allowing a safe margin, was to rotate the pipette so that it made three revolutions in one minute. This is so slow that the pipette must be observed attentively to see that it moves.

A satisfactory degree of dilution is *one* of blood with *nine* of the germ suspension in normal salt solution. This degree of dilution is selected and made a constant, because the leukocyte pipettes in the hands of every laboratory worker allow of this dilution. The introduction of a special instrument is thus avoided, and, in fact, a special pipette could be of no advantage.

SIMPLIFIED METHOD. For the purpose of opsonic work, therefore, we may dilute one part whole blood with nine parts germ suspension in isotonic salt solution in a leukocyte pipette, and rotate it at the rate of thrice a minute in a thermostat at 38° C. for fifteen minutes; at the end of which time we may make our spreads. The spreads, of course, may be stained and counted at any convenient time. The whole process is not materially different from a leukocyte count except for the fifteen minutes in a thermostat. While it takes longer to make an opsonic count than a leukocyte count, the whole process is not longer than of making the count for both reds and whites, and is shorter than a gastric juice analysis or a quantitative urinary.

The leukocytes are distributed throughout the spreads, but are, of

course, found most abundantly along the edges of the smears. The salt solution does not interfere with the normal action of the serum or the normal activities of the leukocytes, and no leukocytes are destroyed or injured by the process.

After blowing out the mixture on slides and spreading, it is desirable at once to wash out the pipette, because with the absence of motion the blood mixture may yet clot, and be difficult to remove from the pipette.

Certain bacteria, such as the colon bacilli, favor clotting and emphasize the necessity of perfect conditions. By perfect conditions I mean pure water, pure salt, clean containers, clean dry pipettes, proper motion, proper heat, and a quick handling of the blood. These points are further emphasized by the wide variations in the "clotting time" of blood from various patients.

MINOR TECHNIQUE. Certain points in the technique, while simple, are important. The finger tip is the most practicable source of blood. After cleaning, it should be punctured with a suitable point so as to obtain a full-sized drop without much pressure. This blood drop should be sufficiently large to fill the pipette

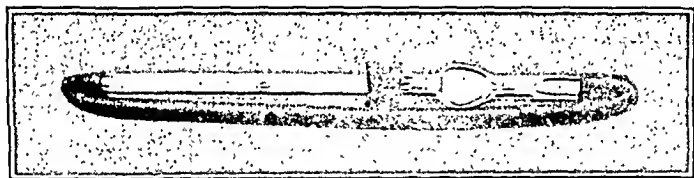


FIG. 1.—Leukocyte pipette filled and ready for clockwork.

to mark I at the first attempt. If the pipette is filled in instalments from several drops, the delay favors clotting before the blood mixture is subjected to the rotary motion of the clockwork. The stem of the pipette should be filled with the germ suspension and then blood drawn in to mark I. The tip of the pipette is wiped clean with a strip of plain gauze (never cotton) and enough of the bacterial suspension drawn into the bulb to fill the pipette to the mark XI. The mouthpiece is slipped out of the rubber tubing, the free end of which is pushed on to the tip of the pipette, as shown in Fig. 1.

The rubber tubing is cut of such a length that it must be gently stretched in order to reach over both ends of the pipette. The filled pipette is then slipped on to the rotating arm of the clockwork as in Fig. 2.

The clockwork with the attached pipette should be placed at once in a thermostat at 38° C. for fifteen minutes. The time between drawing blood into the pipette and placing the clockwork in the thermostat should be constant. One minute gives ample time for this. Care must be taken not to allow the blood mixture to push back into the capillary tube of the pipette as the rubber tubing is being adjusted, or the blood mixture in this portion may clot in spite

of the clockwork and thus interfere with blowing out the blood mixture on the slides. When this is found to have occurred, reverse the pipette and try to blow the blood out at the larger end, when ready to spread the slides.

When the pipette is removed from the thermostat, the rubber tubing is released from one end, a mouthpiece slipped in the free end of the tubing, and half the blood mixture blown out into the waste basin. A drop is then deposited on a clean warm slide and spread in the usual way by drawing the edge of another slide across the drop so as to give a thick even film over the first slide. Two slides should be spread and then dried over the flame at a height endurable to the fingers. The slides, in the case of the tubercle bacilli, may be fixed in methyl alcohol, stained in carbol-fuchsin and decolorized as usual, after which they may be counterstained by Wright's stain or Löffler's alkaline methylene blue. This step

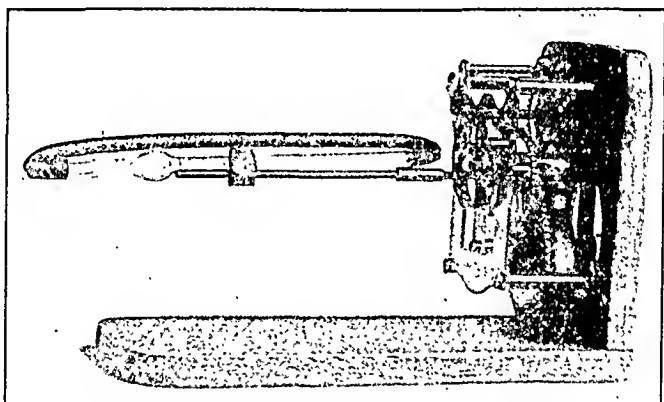


FIG. 2.—Clockwork for revolving pipette.

of spreading and staining takes the same time as spreading and staining sputum. The number of germs in each leukocyte may now be counted under the microscope. Neutrophils, transitionals, and eosinophils only are counted. If the number of bacteria in each leukocyte is written in a column, with a cipher, to record each empty leukocyte, we will have recorded the number of active leukocytes without further effort.

In counting, the rule should be to count any clump of two or more germs as one, because the ingestion of a clump represents probably no greater leukocytic activity than the ingestion of a single germ. If a bacillus is partly in, it is counted as ingested, but germs lying merely in contact with the cell body should be carefully excluded from the count. The error due to germs over or underlying without being within cell boundaries, is ineradicable; but fortunately this error is a negligible quantity, unless the germ suspension be much too thick.

BACTERIAL SUSPENSION. Bacteria distributed in normal salt solution for opsonic work must be free or nearly free from clumps. This is usually accomplished by grinding the germ-mass with a few drops of salt solution in a small agate mortar, then drawing the diluted mixture in and out of a pipette, the square cut end of which is pressed against the bottom of the mortar; and lastly, centrifuging to free the suspension from the few remaining clumps. The resulting suspension still should be sufficiently dense to allow of standardization by dilution. The comparison of the opalescence of the germ suspension with an arbitrary standard, such as a mixture of barium sulphate in water, as proposed by McFarland, is useful as an approximation. The method, however, of using the whole blood in a mixing pipette allows us to make use of an early suggestion, which is, to regulate the number of bacteria in the germ suspension by the number of red cells in the blood. Any whole-blood method presents on each slide a mixture of red cells and the bacteria employed. We have, therefore, on every slide a controlling means of estimating with reasonable accuracy the density of our germ suspension. It may be roughly standardized first by McFarland's method and then the density may be estimated from the stained slides, with due regard to the degree of anemia presented by the patient.

Thus, no slide need be discarded if the suspension is within reasonable limits, because, as has been shown, the number of germs ingested is directly proportionate to the number in suspension. Therefore, by counting a single field of an evenly spread slide, we may estimate the proportion between germs and red cells and correct our count accordingly. This correction is rarely necessary in the case of the per cent. of active leukocytes, because unless the suspension is very thin, this factor suffers variations too slight to be considered.

Unquestionably the most accurate method of standardizing the germ emulsion is to count the bacteria on a Thoma-Zeiss hemocytometer precisely as when standardizing the vaccine for injection. Most bacteria do not remain intact in emulsion, and, therefore, the emulsion for opsonic estimations must be freshly prepared each time.

PRESERVATION OF BACTERIAL SUSPENSIONS. The tubercle bacillus is an exception to this rule. The bacillary body remains intact, but tubercle bacilli in normal salt solution after a few days begin to agglutinate. The use of distilled water and boiling greatly lessens the agglutinative processes, so that, adding the requisite quantity of salt just before using, enables us to make up a standard emulsion of the tubercle bacilli in distilled water, which will remain standard for a month or more, particularly if used every few days and agitated.

To store the tubercle emulsion in distilled water, it is convenient

to use a piece of glass tubing 10 cm. long and 1.5 cm. in diameter with each end drawn out while hot into a long stem, as in Fig. 3. By means of a piece of small rubber tubing and bulb the emulsion may be drawn into this receptacle until it is two-thirds full. Then, without removing the rubber tubing, the free glass stem tip may be sealed in the flame. The rubber tubing may now be removed and the glass receptacle stood upright in the sterilizer. After sterilization the open stem tip may be sealed in the flame. To use the emulsion, shake well, scratch the stem near the tip with a file, break off the tip, hold open tip over a small test-tube and heat the body of



FIG. 3.—*a*, tube of dried salt solution, with or without vaccine; *b*, storage tube for tubercle emulsion.

the emulsion gently with the flame until the required quantity has been forced out by heat expansion, after which the tip may again be sealed in the flame without re-sterilization being necessary.

Instead of adding a weighed quantity of salt to each measured test-tube of emulsion, it is convenient to make up a quantity of isotonic saline, pour from 1 to 3 c.c. into each of fifty or more small flat bottom test-tubes, mark with a file the height of the fluid in each tube, place all in sterilizer, evaporate to dryness and plug with sterile cotton. When the tubercle emulsion in distilled water is flowed into one of these tubes so as to fill it to the file mark, the salt already in the tube makes an accurate normal solution without trouble or loss of time. (See Fig. 3.)

As a method of preserving a bacterial emulsion for estimating the opsonic index until counted, we evaporated to dryness a bacterial

emulsion in normal saline. We hoped that by adding distilled water to the file mark, the original emulsion could be restored. The method was not successful, because tubercle bacilli became agglutinated to some extent, and because other species of bacteria were more or less disintegrated.

PRESERVATION OF BACTERIAL VACCINES. This method is ideal, however, as a means of preserving bacterial vaccines easily and indefinitely without deterioration. The bacterial suspension should be made in 0.8 sodium chloride solution and standardized to a definite number of bacteria per cubic centimeter. A maximum dose should then be poured into each of any desired number of small flat bottom test-tubes (Fig. 3). The height of the fluid in the tubes should be marked with a file. The tubes should be evaporated to dryness at from 50° C. to 60° C., and plugged with sterile cotton. Each tube will thus contain a measured dose of non-living bacterial substance dried in salt. In this state it will remain sterile and unchanged indefinitely.

To use a tube of dried vaccine, fill to the file mark with sterile water. A little agitation with a sterile platinum wire gives a suspension in a few seconds because of the solubility of the salt. This suspension may now be drawn into a sterile syringe and the maximum dose or any part thereof injected subcutaneously. We are thus enabled to sterilize and preserve autogenous bacterial vaccines in a permanent and convenient form without antiseptics of any kind, unless common salt be so considered. This method does not apply to the preparation of tubercle vaccine. Here the emulsion of the ground germ substance is to be preferred.

DENSITY OF SUSPENSIONS. By the rotary whole blood method, using a dilution of 1 in 10, there should be 1 germ to 25 red cells. The dilution employed enables us to use this proportion with the staphylococci and bacteria in general without finding the cells too crowded with bacteria for accurate counting. In the case of tubercle bacilli 1 germ to 100 reds makes a satisfactory density. The allowed variation in the number of red corpuscles ranges from 5,000,000 to 3,000,000. If lower than this, the anemia would be too evident not to demand a "blood count." Therefore, it is practical to allow a proportionate variation in the density of the germ suspension without correction.

POOLS AND CONTROLS. The factors which relieve us from control by a pool serum are: (1) The use of an undisturbed hemic system—leukocytes and serum of the same individual without separation. (2) A technique so simple that it can be repeated without variation each time that the opsonic and phagocytic factors are determined. (3) A table of human opsonic and phagocytic factors in health, to show the normal range for various species of bacteria. (See Table I.) (4) An improved notation whereby the opsonic and phagocytic factors are directly stated without the use of a divisor.

TABLE I.—*Normal Opsonic Factors.*

Species of bacteria.	Tubercle bacillus.		Staphylococcus pyogenes albus or aureus.		Bacillus viride.		Colon bacillus.	
	No. of germs per leukocyte.	Per cent. of active leukocytes.	No. of germs per leukocyte.	Per cent. of active leukocytes.	No. of germs per leukocyte.	Per cent. of active leukocytes.	No. of germs per leukocyte.	Per cent. of active leukocytes.
Case No.								
1	0.94	68	7.89	96	0.88	56	6.02	98
2	1.03	63	6.72	92	1.30	70	5.18	96
3	0.92	58	3.00	92	6.00	100		
4	1.06	70	6.48	100	3.10	95		
5	1.20	62	2.70	100	1.80	90		
6	0.92	66	3.34	92	4.50	90		
7	1.06	64	7.00	100	2.04	90		
8	0.94	62	2.40	80	3.48	96		
9	1.00	68	7.24	100	2.12	72		
10	1.06	70	4.70	100				
11	0.76	62	5.40	90				
12	1.16	90	3.72	100				
13	1.48	86	5.64	100				
14	1.40	96	3.08	96				
15	1.46	92						
16	0.80	52						
17	1.06	60						
18	1.92	90						
19	0.68	54						
20	1.24	94						
21	0.96	60						
22	1.30	75						
23	1.06	70						
24	0.88	60						
Average	0.8-1.2	55-75	4-6	90-100	2-4	70-90		

Wright's method is particularly designed to give only the opsonic power of the serum of the patient. The use of an undisturbed hemic system, namely, the whole blood, gives us the opsonic power of the serum plus the native phagocytic power of the leukocytes. The whole blood method, therefore, gives the truer index of an individual immunity. That both serum and leukocytes have greater power in unseparated blood than after separation and re-combining is apparently demonstrated in Table II, where results by the whole blood method are compared with results by Wright's method. It will be observed that the resulting figures are nearly parallel notwithstanding the fact that in the whole blood method the serum is diluted 1 in 20 and in Wright's method the serum of the same patient is diluted only 1 in 3.

TABLE II.—*Comparison of Results.*

Wright's method.			Whole-blood method.	
Germ emulsion, 1 in 3. Serum, 1 in 3. Leukocytes, 1 in 3.		Germ emulsion same in each method.	Germ emulsion, 9 in 10. Serum, 1 in 20. Blood cells, 1 in 20.	
Averages.		Species of bacteria.	Averages.	
No. of bacteria per leukocyte.	Per cent. of active leukocytes.		No. of bacteria per leukocyte.	Per cent. of active leukocytes.
1.12	61	Tubercle bacillus	0.8-1.2	55-75
3.34	92	Staphylococcus pyogenes albus	4-6	90-100
		Colon bacillus	3-5	60-80
2.02	89	Bacillus viride	2-4	70-90

AT THE BEDSIDE. Most of the work will be done in the office, where a thermostat is in constant readiness. But no difficulty is encountered in preparing, by this method, opsonic slides at the bedside of any patient, after which they may be stained and counted at leisure. To this end I have constructed the portable thermostat, 5½ x 8½ x 4 inches, as here shown. This thermostat has a case to prevent the radiation of heat, after the fashion of a fireless cooker. If 1200 c.c. of hot water at 50° C. is poured into the space between the walls of this thermostat it will raise the temperature within to 38.5° C., or about. In the course of a few minutes it sinks about 0.5°, when it remains nearly constant for about half an hour. This allows us the fifteen minutes' use which we require. If the physician is going to the house of his patient within an hour he may fill the walls of the thermostat with water at about 54° C., and have everything ready for immediate use at the bedside, the thermostat serving as a convenient carrier and warmer for all needed apparatus (Fig. 4).

We have to consider variations in the opsonic factors due to difference in virulence of the same germ or to confusion of unrecognizable species. I am not yet prepared to state what these variations amount to, but errors due to the above causes would not apply to the rise and fall of the opsonic index in a series of estimations in the course of any given case. If, in certain cases where the identification of a culture is doubtful, a control is desired, the pool may be used in the rotary whole blood method more easily than by the usual method of collecting the blood of different persons separately, centrifugating and mixing the sera. The blood pipette is so divided that we may conveniently use the blood from two normals for the pool blood without danger of premature clotting; or, we may run

through simultaneously a number of opsonic pipettes, with the same clockwork, by having clips on the revolving rod, on which two, three, or more pipettes may be slipped. The control bloods may then be mixed to form the pool before making a spread.

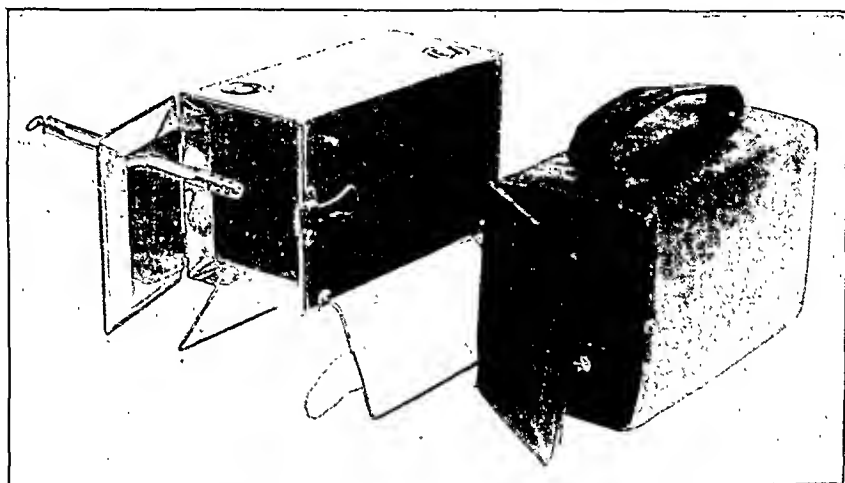


FIG. 4.—Small thermostat with heat-retaining case for use at bedside,

IMPROVED NOTATION. The prevailing method of recording results is open to criticism. The opsonic index is a figure obtained by dividing the average number of germs counted per leukocyte by the normal number per leukocyte. This presupposes a fixed normal (obtained by testing a pool), which can be represented by a single figure. Now, as a matter of fact, there is no such a thing as a fixed normal represented by a single figure. We cannot say that the normal opsonic index for the staphylococcus is 4 any more than we can say that the normal pulse is 72. What we can say is that the normal staphylococcus index is from 4 to 6, just as we may say that the normal pulse is from 60 to 80, or the normal leukocyte count from 3000 to 10,000. But, aside from the absurdity of stating the normal as a definite figure, the whole method of statement is obscure and without analogy to any other laboratory or clinical record.

It is obscure because a chart of opsonic indices gives no clue to the real factors from which it is derived; namely, the actual bacterial average per leukocyte or the normal figure used as a divisor. It is without analogy, because if Wright's opsonic notation were applied in general to clinical work, we would have the specific gravity of a 1015 urine recorded as 0.9950+, which would be a figure obtained by dividing 1015 by 1020 as a normal. Instead of reading the temperature of a patient as 102.5° F., we would be confronted by 1.039+, which would be 102.5°, divided by 98.6° as a normal. A similar arithmetic would protect from uninitiated eyes the record of the pulse, respiration, blood-pressure, the grade

of a leukocytosis or the hydrochloric acidity of the gastric juice. Thus would we draw a mathematical veil over our laboratory findings. If this be found objectionable, why then make an Isis and Osiris of our two opsonic factors?

The two original opsonic factors referred to are: (1) the number of germs per leukocyte, and (2) the number of leukocytes exhibiting phagocytosis. The first could fairly retain the term *opsonic index*, and the second has already received the name of *phagocytic index*. But to avoid confusion of terms, it will be best to speak of the *opsonic factor* and the *phagocytic factor*, leaving the term *opsonic index* to the undisputed use of those who may still prefer the original nomenclature.

After using, since March, 1907, this simplified method of estimating the opsonic and phagocytic factors, I am prepared to maintain: (a) that it brings the opsonic and phagocytic estimations within reasonable time limits as a laboratory procedure in practical medicine; (b) that it increases the accuracy of the results, by making all factors constants, excepting the blood of the patient; (c) that it gives a practical method of correcting on each slide variations in the density of the germ emulsion; (d) that it gives on one slide in the same count both the opsonic and phagocytic factors of the same individual; (e) that no pool is required; (f) that no physical or chemical injury is sustained by either leukocytes or serum; (g) that it may be used with equal facility at office or bedside. If other workers can substantiate these results, I believe that the estimation of opsonic and phagocytic factors will take its place beside other laboratory methods of recognized practicability.

I have to thank my assistants, Dr. Lloyd Howe and Dr. C. M. Spencer for their cheerful and careful work of counting slides and otherwise helping me in carrying out this work amid the distraction of private practice.

REVIEWS.

THE AFTER-TREATMENT OF OPERATIONS. By P. LOCKHART MUMMERY, F.R.C.S. (Eng.), B.A., M.B., B.C. (Cantab.), Senior Assistant-Surgeon, St. Mark's Hospital, etc. Third edition: pp. 251; 38 illustrations. New York: Wm. Wood & Co., 1909.

IN this edition of this excellent little book, alterations have been made to the chapters on abdominal surgery, genito-urinary and rectal operations, and there has been added an article on the treatment of cases of general peritonitis, and on the serum and vaccine treatment of sepsis. The chapter on shock has been revised and brought up to date. An introductory chapter upon the position of the patient, thirst, flatulence, bed-sore and postoperative mania, is followed by some excellent pages upon the treatment of the wound and its complications. The chapter upon shock is perfectly up to date, as is to be expected from the eminence of the author in this field. In the description of the treatment of vomiting after operation several pages are devoted to a variety of drugs and counter-irritants, most of which might have been omitted, as frequently repeated gastric lavage is more satisfactory than any other treatment. The remainder of the book is devoted to the description of the after-treatment of operations on the abdomen, genito-urinary tract, joints, etc., to which is appended a short chapter on rectal feeding.

G. P. M.

A TREATISE ON ORTHOPEDIC SURGERY. By ROYAL WHITMAN, M.D., Assistant Professor of Orthopedic Surgery in the College of Physicians and Surgeons of Columbia University, New York; Associate Surgeon to the Hospital for Ruptured and Crippled, etc. Fourth edition, revised and enlarged. Pp. 908, with 601 illustrations. Philadelphia and New York: Lea & Febiger, 1910.

THE enlargement of the present edition of Dr. Whitman's justly popular *Treatise on Orthopedic Surgery* is greater than is indicated by the increase in number of pages from 871 in the third edition to 908 in the present, since by rearrangement of display type, para-

graphing, etc., considerable space has been gained. The number of illustrations has been increased by 47.

Among the subjects discussed for the first time in the present edition, the following have arrested the reviewer's attention: Calot's method of gradual correction of the deformity in Pott's disease by means of plaster jackets; the use of Beck's bismuth paste in sinuses, etc.; vaccines in gonorrhoeal arthritis; and Volkmann's ischemic contracture. The sections dealing with "quiet effusion" of the knee-joint (classed by some as a vasomotor neurosis), and those describing the operative treatment of obstetrical palsy, have been enlarged. No mention has been found of formalin-glycerin injections in cases of arthritis.

There is apparent an increased liking on the author's part for plaster-of-Paris dressings instead of braces. He still advises the use of an Esmarch band in all operations on the knee- and ankle-joints (excision, arthrectomy, arthrotomy, and arthrodesis). There is a glaring typographical error at line 13 of page 400.

This edition is without doubt an improvement on what was already a good work, and assures to the *Treatise* a continuance of that favor with which it has long been received by students and practitioners of orthopedic surgery.

A. P. C. A.

THE SURGERY OF CHILDHOOD, INCLUDING ORTHOPEDIC SURGERY.

By DE FOREST WILLARD, M.D., Professor of Orthopedic Surgery in the University of Pennsylvania. Pp. 800; 712 illustrations, 17 in colors. Philadelphia: J. B. Lippincott Company, 1910.

It is a source of profound regret that the author of this admirable treatise should not have lived to appreciate and enjoy the welcome it is sure to receive from the profession. The book reflects the experience and the accumulated knowledge of a long and industrious life. It is comprehensive—almost encyclopedic—but it reveals throughout the conviction and judgment that come exclusively neither from practice, nor from reading, nor from teaching, but from the combination of all three that gives the widest outlook on surgical as on other sciences. It cannot be pretended that a reviewer who was bent on disagreement or on finding deficiencies would be altogether unsuccessful; but, under the circumstances, this function may be ignored, in the presence of so very much that deserves commendation and so very little that is open to unfavorable criticism. It is certainly true that no one book with which we are familiar contains so much information as to the surgical conditions of childhood, and none can, on the whole, be more

safely followed in practice. If Dr. Agnew were living he would be glad to accept the dedication in which Dr. Willard in well-chosen words recalled his memory.

J. W. W.

DISEASES OF INFANCY AND CHILDHOOD. THEIR DIETETIC, HYGIENIC, AND MEDICAL TREATMENT. By LOUIS FISCHER, M.D., Attending Physician to the Willard Parker and Riverside Hospitals, New York City. Third edition; pp. 980; 303 illustrations. Philadelphia: F. A. Davis Company, 1910.

A CAREFUL perusal of Dr. Fischer's well-known text-book confirms the favorable opinion created at its first publication. The present volume, according to the preface, has been submitted to a thorough revision; from the facts that no increase has been made over the original number of pages and that the folios correspond almost invariably in the two editions, we must conclude that very little could have been found in the earlier edition to call for change. The most noticeable additions have been made in the section covering the treatment of epidemic cerebrospinal meningitis, which now includes the technique of administration of Flexner's serum. To the original very valuable article on Infant Feeding the caloric method has been added and a new method for preserving human milk is described. In septic diphtheria the intravenous injection of antitoxin is now advocated, and for hemophilia the value of injections of horse serum is praised and its use after tonsillotomy is favored. Short sections on scabies, indicanuria, pyuria, acetoneuria, and diabetes are added to make good earlier omissions, and some changes and substitutions in the illustrations complete the revision. The book offers a very satisfactory text-book on the subject of children's diseases, and is especially interesting for the personal note that echoes the mature judgment and wide clinical experience of its distinguished author.

T. S. W.

MEDICAL EXAMINATION OF SCHOOLS AND SCHOLARS. Edited by T. N. KELYNACK, M.D., F.R.C.P. (Lond.), Honorary Physician to the Mount Vernon Hospital for Consumption and Diseases of the Chest, England; with an introduction by SIR LAUDER BRUNTON, Bart., M.D., D.Sc., LL.D. (Edin.), F.R.S. Pp. 434. London: P. S. King & Son, 1910.

To those who may still entertain a doubt as to the importance of, and the urgent necessity for, the medical examination of school children, this book, edited by Kelynack, is earnestly recommended.

No one can read the book without being impressed by the world-wide character of the movement which, within the past decade, has brought the younger students, at least of nearly every civilized nation, under some sort of medical supervision. The work consists of a collection of thirty-two papers, dealing with every aspect of the medical examination of scholars, from the youngest children in the primary schools to the more mature inmates of the great English public schools and American colleges. The contributors are in every instance experts, well qualified from personal experience to write with authority upon their respective subjects.

Fully a third of the book is devoted to a discussion of the various problems which confront the educational and health authorities of England since the passage of the Educational Act of 1907—an epoch-making law which for the first time established compulsory systematic medical examination in the public elementary schools. However interesting these considerations may prove to Englishmen, they furnish but dull reading for the foreigner unfamiliar with English systems of education and municipal control. It is evident, however, that the editor has been alive to this fact, and, furthermore, he has appreciated the significance of the assertion made in the introductory chapter by Sir Lauder Brunton, that the cause of the child is a cosmopolitan one. Consequently, Kelynnack has enlisted the services of representative men from all the nations that are leaders in educational advancement and has had them contribute chapters upon the status of the medical examination of school children in their respective countries. Moreover, the sections dealing with methods of routine medical examination of scholars, the examination of the organs of special sense, the dental conditions found in school children, and the management of mentally defective children have happily been written upon such broad lines, and contain so many valuable suggestions, that they cannot fail to prove useful to all, regardless of nationality, who are interested in the welfare of children.

The report upon the medical examination of school children in the United States has been furnished by such well-known workers in this field as Gulick and Ayers. From their observations it would seem that the status of this work in the United States today compares favorably with that which is being done by other great nations. There is occasion for some satisfaction when we learn that nearly ten years before the recent English Education Act was passed the four great cities of New York, Chicago, Philadelphia, and Boston had adopted systematic methods for the medical inspection of schools. The unique problem of physical education in American universities is dealt with in an entirely separate chapter by R. Tait McKenzie.

In spite of the fact that much of the contents of the book applies more particularly to conditions in England, the desire of the editor

to furnish a work of international scope has been fulfilled. Although the book will doubtless appeal more directly to educators and school medical officers, it should also prove of real interest to all who adequately appreciate the far-reaching importance that the health of the child bears to national development.

G. M. P.

CLINICAL OBSTETRICS. By ROBERT JARDINE, M.D., M.R.C.S., Professor of Midwifery in St. Mungo's College, Glasgow. Third edition; pp. 717; 112 illustrations. New York: William Wood & Co., 1910.

DR. JARDINE has prepared a book which is extremely interesting from several points of view. First of all, it is written in the first person singular, or, in other words, it is the expression of his own experience and his own judgment as based upon that experience; second, it is written in what may be called the conversational style; and third, he has included a vast number of illustrative case-histories as explanatory or corroborative matter. For each and all of these peculiarities he is to be thanked. It is refreshing to the mental palate to have the daily obstetrical diet made appetizing by condiments such as these. The verdict of the medical public is attested by the fact that this is the third edition since 1903, and while this alone is not absolute proof of the worth of this or any other volume, it is, at least, strongly presumptive, and in this instance careful reading will amply sustain the favorable opinion of the previous editions. The whole subject of obstetrics is well covered, and the only criticisms concern relatively minor points. For instance, more space might well have been allotted to the consideration of pyelitis as a complication of pregnancy, particularly with regard to the etiological theories and the differential diagnosis. In this connection it may be noted that the statement that recurrence in the same pregnancy is rare does not accord with the experience of many observers. It would have been better, in view of the importance of the matter and the casual attention given to it by the general practitioner, to have insisted upon the necessity of an internal, in addition to the external, examination before labor in all primiparæ. One of the best parts of the book is the chapter of fifty pages devoted to eclampsia. It is a great satisfaction to note the prominence awarded to venesection in the consideration of the treatment of this grave complication. The author is particularly to be congratulated in that he is not afraid to bleed even those patient who do not present an excessive blood pressure. The Bossi dilator, however, should not be mentioned as a means of *accouchement forcé*, as this instrument certainly has no place in the armamentarium

of the general practitioner. The method of suture of the uterine wound after abdominal Cesarean section leaves room for improvement. Through-and-through sutures, while unquestionably successful in a large series of cases, do not offer the ideal method here any more than in the closure of the abdominal parietes. The criticisms just made are all which can be brought forward against the subject matter of this book, while on the other hand, the limits of a review prevent any just consideration of its merits. Suffice it to say that it is one of the most interesting and valuable systematic expositions of obstetrics published within recent years. W. R. N.

A MANUAL OF HUMAN EMBRYOLOGY. Edited by FRANZ KEIBEL, M.D., and FRANKLIN P. MALL, M.D. Philadelphia and London: J. B. Lippincott Company, 1910.

IN this first volume of the new *Manual of Human Embryology*, edited by Keibel and Mall, and appearing simultaneously in Germany and America, the editors have been most fortunate in securing contributions by the most prominent embryologists in this country, Germany, and Austria. The authors of chapters on different subjects are: Bardeen, of Madison; Evans, of Baltimore; Felix, of Zurich; Grosser, of Prague; Keibel, of Freiberg; Frederick T. Lewis, of Boston; Warren H. Lewis, of Baltimore; McMurrich, of Toronto; Mall, of Baltimore; Minot, of Boston; Pinkus, of Berlin; Florence Sabin, of Baltimore; Streeter, of Ann Arbor; and Tandler and Zuckerkandl, of Vienna.

The introductory chapters on germ cells, fertilization, segmentation, young human ova and embryos, the formation of the germ layers and gastrulation, and the summary of the development of the human embryo are by Keibel, and form a notable contribution to our knowledge of these imperfectly known and disputed subjects. Unfortunately, the lucidity of many passages in these first chapters is greatly impaired either by imperfect translation or by the difficulty of translating with any degree of clearness the involved diction of the original German. This is particularly noticeable in the fine print. A painstaking tabulation and careful description of the youngest known human ova is a valuable feature of this part of the work, and the illustrations and reproductions of photographs are very happily chosen. We could wish particularly that Keibel had been more definite in his description of the process of gastrulation and the formation of the germ layers and notocord, and that he had devoted more space to his descriptions of fertilization and segmentation. In the chapter on the development of the egg membranes, the placenta, and menstruation by Grosser, the text is both concise and clear, and the illustrations are a valuable supplement to the text.

The chapters on the determination of the age of human embryos and fetuses, the pathology of the human ovum, and the development of the celom and diaphragm by Mall, form a scholarly, lucid, and detailed account of the subject matter. Many of the facts brought out by Mall are new, as are a large number of his illustrations. His chapter on the pathology of the human ovum opens up a field of which very little is known, and is perhaps the best statement of the etiology and fate of abnormal ova and embryos extant.

The chapters on the development of the skeleton and connective tissues, by Bardeen, and the development of the muscular system, by Lewis, while clear and lucid, are too elaborate for the use of any but those especially interested in embryological or biological research. They form a concise and yet comprehensive resume of the development of these systems, and the illustrations are, to a large extent, new and original—always a favorable feature in a work of this kind.

If the second volume of the book maintains the standard set in the first, the book will rank with those of Minot and Hertwig as one of the best books on the subject. No treatise on embryology since the works of Minot and Hertwig appeared shows such careful and painstaking search of the literature on the subject, or wealth of new material in the way of results of original investigation, as does this monumental work of Keibel and Mall and their co-elaborators. A particularly pleasing feature of the book is the absolute candor with which the authors repeatedly admit their inability to explain certain phenomena or processes on account of the general lack of knowledge of the subjects involved. In view of such admissions, and they average one or two to the page throughout the book, it seems strange that so comparatively few investigators have been attracted to the research of a subject so broad, so intensely interesting, and so replete with virgin opportunity.

H. H. C.

LEITFADEN DER EXPERIMENTELLEN PSYCHOPATHOLOGIE. By Privatdozent DR. ADALBERT GREGOR, Oberarzt der Psychiatrisch-Neurologischen Klinik, Leipzig. Pp. 222. Berlin: S. Karger, Karlstrasse, 15, 1910.

THIS is an excellent presentation of the present status of experimental psychopathology. It is in a series of sixteen lectures, delivered in the Leipzig school. It takes up the subject of the pathology of psychological conditions, not in an anatomical but in a true mental sense. It is impossible to review this work because it encompasses so much, but it is written in such a manner that the results of the experiments are compared in the normal and abnormal.

T. H. W.

THE HYGIENE OF INFANCY AND CHILDHOOD. By A. DINGWALL FORDYCE, M.D., F.R.C.P. (Edin.), Extra Physician to the Royal Hospital for Sick Children, Edinburgh. Pp. 289; New York: Wm. Wood & Co., 1910.

DR. FORDYCE has made a distinct departure from the time-honored methods of discussing the hygiene of early life. In his own words, the work "professes to correlate the primary scientific facts of medicine as they apply especially to pediatrics."

This attempt within the limits of a small volume would, *a priori*, necessitate an incomplete presentation, but the author has succeeded admirably both in the selection of topics and the avoidance of moot points for discussion.

The book is divided into five parts: Part I describes the factors involved in nutrition, including metabolism, both normal and pathological. In Part II are considered the problem and clinical aspect of heredity. Part III takes up the factor of environment, and Part IV the bacterial factor. Part V concludes with a consideration of the factors which vary according to the age-period. From this brief synopsis it will be seen that the author has given a broad, comprehensive view of child-welfare rather than a detailed description of methods of child-raising.

Diet is considered mainly from the standpoint of metabolism, including also much practical instruction in feeding. The method of describing the effects of food according to its component parts is in line with modern teaching. The problems of metabolism are judiciously presented in that only generally accepted facts are made use of. The subjects of heredity and environment receive more adequate consideration than is usual in general, as opposed to neurological, pediatric literature. The presentation of the bacteriological factor in health and disease is conservative. None but the well recognized and best attested infections are considered.

The division of Part V into age-periods, each with its effect upon the child's physical and moral welfare, necessitates occasional repetition, but is well justified.

For the student of pediatrics, the full bibliography will be of value. It may also be permitted to congratulate the author upon his very frequent use of the quotation mark—honor everywhere being given to whom it is due. Recognizing the aims of the author and the limitations of space, the only criticism which suggests itself is that the problem of the nervous or neurotic child receives hardly enough consideration. The book deals with the dangers which beset the normal child, and, from that standpoint, discusses the factors which tend to produce an unstable nervous system. Such a large proportion of children at the present day are neurotic almost from birth that their management deserves special consideration in any work laid down within the general outlines of the present volume.

Since the author's experiences probably do not include many with the *Puer et Puera Americana*, the neurotic problem may not have impressed itself so strongly upon him as upon his American confrères.

In conclusion, it may be said that the special value of the book lies in its stimulus to the consideration and study of the larger factors involved in the child's development.

J. C. G.

HYPNOTISM. By H. E. WINGFIELD, M.A., M.D., B.C., Cantab., Consulting Physician Royal Hants County Hospital, formerly Demonstrator of Physiology in Cambridge University. Pp. 175. New York: William Wood & Co., 1910.

THIS small book is intended for those who know nothing of hypnotism, and is therefore very elementary. It is questionable whether there is really need at the present time for a work on this subject, because hypnotism has become largely into disrepute as a method of treatment. Again, elementary works upon this subject do more harm than good because hypnotism, if it is employed at all, should be used by men who are trained in such work and such men need no elementary books. The subject itself is well handled. The author is very conservative, but here and there creep in statements of cures of certain diseases by hypnosis which to the average practitioner who handles such cases seem somewhat remarkable.

T. H. W.

DIE PARALYSIS AGITANS. DR. KURT MENDEL, Nervenarzt in Berlin. Pp. 106. Berlin: S. Karger, 1911.

THIS is an excellent review of our present knowledge of paralysis agitans. The author has carefully compiled the literature and discusses the clinical and pathological symptoms. He comes to no new conclusion. In discussing the etiology of the disease he states that the cause is not known, but that it is probably the result of a disease of the motor columns resulting from an arterial basis.

T. H. W.

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Globulin Content of Luetic Sera.—R. MULLER and W. R. HOUGH (*Wiener klin. Woch.*, 1911, xxiv, 167) have repeated Winternitz's work on the globulin content of luetic sera. The sera were controlled by Wassermann reactions. Two hours after obtaining the blood from a vein in the arm it is centrifugalized till the serum is clear. The latter is divided into two portions. To the one there is added one part of a saturated aqueous solution of ammonia sulphate to two parts of serum, to precipitate the euglobulin; to the other an equal volume of saturated ammonium sulphate is added to throw out of solution the total globulins. The amount of protein is estimated by centrifugalization in graduated tubes, noting the bulk of the precipitate. Muller and Hough report observations on 58 sera, 29 of which were luetic, the remainder non-luetic controls. In the luetic sera the euglobulin amounted to 42.5 parts (calculated for 10 c.c.); in the controls, 28.8. Total globulin showed less variation, 94 in luetic sera, 84.7 in the controls. Constant results were not obtained, wide variations being noted.

Transmission of Antipyrin Idiosyncrasy to Guinea-pigs.—E. KLAUSNER (*Münch. med. Woch.*, 1911, lviii, 138) has successfully repeated Bruck's experiments. A patient with neurasthenia, male, aged twenty-nine years, came under Klausner's care; since childhood he had shown an idiosyncrasy for antipyrin, manifested by marked erythema and œdema of the skin and formication, especially of the skin of the head.

Blood serum obtained from this patient was injected, in 5 c.c. amounts; into each of three guinea-pigs (Nos. 1, 2, 3). A fourth guinea-pig received a like quantity of serum from a normal individual, and a fifth received no serum. Twenty-four hours later 0.3 gram of antipyrin was given to the guinea-pigs subcutaneously. In the course of an hour the first animal was attacked with clonic-tonic spasms, and died in a few hours. The second animal succumbed with similar symptoms. The controls, animals 4 and 5, showed no ill effects from the drug. Eight days after injecting the serum, guinea-pig No. 3 and two new controls were each given 0.3 gram of antipyrin subcutaneously. The controls were unaffected. The reaction in animal No. 3 was extreme; clonic-tonic spasms began during the injection of the antipyrin. There was not, however, as in the first two animals, a fatal issue, the animal having recovered fairly in twelve hours. The reaction is very similar to, if not identical with, the anaphylaxis reaction.

Myeloid Chloroma.—E. PAULICEK and L. WUTSCHER (*Deutsche med. Woch.*, 1911, xxxvii, 155) report a case of chronic myeloid leukemia which had been under their observation since 1907. Before death unusual manifestations of chloroma were noted and confirmed at autopsy. They summarize their findings as follows: (1). The records of this case show that chronic myeloid leukemia may change into chloroma. Previously, myeloid chloroma has been observed only in association with acute leukemias. (2) The development of chloroma from a preëxistent chronic myeloid leukemia bears witness to the close relationship between the two disease processes. (3) The development of an acute chloromatous condition may be without effect upon the blood picture of a preëxistent chronic leukemia. (4) It is possible that the green color of the infiltrations is intimately associated with the rapid proliferation of unripe marrow cells (myeloblasts), though this remains to be proved. (5) It is furthermore possible, Paulicek and Wutscher say, that radiotherapy in some way was responsible for the development of the chloromatous process.

Familial Diabetes Mellitus.—TH. LANGAKER (*Deutsche med. Woch.*, 1911, xxxvii, 217) reports a remarkable diabetic family of children. The parents, Swedes, aged about fifty years, had emigrated to Norway, where all of their children were born. Each of the parents was in good physical condition, had no glycosuria, and denied luetic infection. Their respective family histories were good and were negative for diabetes. Of their eight children, five died between the ages of four and eleven years of diabetes mellitus. Langaker attended three of the fatal cases. Their first child died in 1889, aged twenty months, from diphtheria. In 1897, their four-year-old son became ill with diabetes mellitus. He was admitted to hospital, where the diagnosis was made, and died after a few months' illness. Except for whooping cough and measles, he had been healthy previous to the onset of diabetes. Autopsy revealed no adequate lesion; the pancreas showed little change. In 1899 a second son, aged four years, died of diabetes mellitus. He had had "inflammation of the brain" when one year old. No autopsy was

permitted. The same year a daughter, aged eleven years, began to manifest the usual symptoms of diabetes mellitus. Ten months later she died in diabetic coma (no autopsy). She had had pertussis at the age of two years, and chickenpox shortly before the onset of diabetes. In 1901 a daughter, aged four years, developed all the symptoms of diabetes shortly after recovery from measles, and died in coma in June of the same year. A son, aged seven years, had had diphtheria at the age of five. Langaker was called to see him in September, 1906, and found the child in diabetic coma (glycosuria, acetonuria); he died a few days later. Autopsy revealed diffuse degenerative changes in the glandular cells of the pancreas, including the islands of Langerhans. At present two healthy children remain, aged seven and five years.

The Action of Salvarsan in Malaria.—J. IVERSEN and M. TUSCHINSKI (*Deutsche med. Woch.*, 1911, xxxvii, 107) have used salvarsan in 61 acute malarial infections, of which, 24 were tertian, 3 quartan, 29 estivo-autumnal, 2 mixed tertian and estivo-autumnal, 1 mixed quartan and estivo-autumnal, and in 2 no parasites were demonstrable. In general their results coincide with those of other observers. They report that: (1) Salvarsan, given once intravenously in 0.5 gram dose, exhibits a specific action on all species of malarial plasmodia. (2) In tertian fever the parasites disappear from the blood usually after twelve to forty-eight hours, and the paroxysms cease. How permanent the result is, remains to be seen. It is advised to combine intramuscular with intravenous injection. (3) In quartan fever the benefit from salvarsan is transient, even with a dose of 0.8 gram. (4) Doses of 0.5 to 0.8 gram free the blood of estivo-autumnal parasites only temporarily. (5). Crescents do not disappear from the blood, but they occasionally show change in form and staining reaction for a short time following the injection. (6) In certain cases of estivo-autumnal fever, after a temporary disappearance of the ring forms, with lowering of the body temperature, the patient seemed actually worse and the blood was swarming with ring forms and crescents.

The Albumin Reaction in the Sputum.—M. GANTZ and R. HERTZ (*Berlin klin. Woch.*, 1911, xlviii, 285) emphasize the value of testing the sputum for albumin, a procedure which has been found useful by a number of observers, notably Bezançon and de Jong, Roger, and Wanner. *Method:* A mixture of sputum, 10 c.c., distilled water, 10 c.c.; 30 per cent. acetic acid, 2 c.c., is stirred thoroughly with a glass rod till the sputum is broken up into fine particles. It is then filtered. The filtrate is usually clear, occasionally slightly opalescent, and generally is colorless, at times yellowish. The filtrate is boiled. If the fluid is not too acid, a precipitate of albumin appears. If the acidity is too high—and this is often the case—alkali is carefully added drop by drop and the precipitate then comes down. Occasionally, as Wanner has shown, the addition of a few cubic centimeters of concentrated sodium chloride solution makes the reaction sharper. Gantz and Hertz consider the albumin reaction of great value, since it is practically

pathognomonic of inflammation or œdema of the lungs. In pure bronchial catarrh the test is always negative. In pulmonary tuberculosis (except probably fibroid phthisis) the reaction is positive, even in the early stages. The albumin test may be positive before bacilli appear in the sputum, and with suggestive signs or symptoms may clinch the diagnosis. In pneumonia and pulmonary infarct the test is always positive, likewise in œdema of the lungs, even of slight degree.

An Investigation into the Pathological Physiology of a Case of Clinically Cured Cirrhosis of the Liver.—While there are several cases of clinically-cured cirrhosis, necropsy has always shown definite lesions, which are of comparatively small importance if the liver functionates properly. RIBIERE and PARAF (*Société Médicale des Hôpitaux*) studied a man, aged sixty-six years, with a pronounced alcoholic history, who had cirrhosis and had been tapped forty-seven times up to 1907; in 1910 he came back to the hospital, apparently cured. There was no ascites, digestive or urinary disturbance; no collateral circulation visible; slight hemorrhoids. He had no alimentary glycosuria subsequent to taking 150 grams of levulose, but the excretion of methylene blue was prolonged and intermittent. There was no diuresis, following large amounts of water, and the excretion of chlorides was much delayed. There were no urobilin or bile pigments in the urine. It is thus apparent that there is a certain degree of portal hypertension, and that the liver cells are definitely damaged. Chauffard and Castaigne are led to attribute great importance to the excretion of methylene blue as a functional test for liver sufficiency. The alimentary glycosuria test is, on the contrary, so full of uncertainties as to not be reliable at all. These tests show that the hepatic cells are damaged, and while the patient is clinically cured, he must be maintained upon a rigid régime to prevent a relapse. An interesting point is that, clinically, this was a case of atrophic cirrhosis, and most of the apparent cures have been in cases of large livers. This cure must be laid to the rigid diet of milk and the associated absolute repose.

Treatment of Addisonian Anemia with Salvarsan.—BYRON BROMWELL (*Brit. Med. Jour.*, 1911, i, 547) reports two cases of the so-called pernicious or Addisonian anemia treated with "606;" after noting the fact that those cases do best which take large doses of Fowler's solution and are in the early stages, he shows that one was taking 36 and the other 27 drops of Fowler's per diem. After two months of treatment in one case and one month in the other, the Fowler's solution was stopped and four doses of "606" (each dose 2 to 3 grams) administered to each patient at approximately two weeks intervals. While in the Fowler's solution treatment there had been slight improvement, the change after "606" was marked. The hemoglobin, which had increased from 30 to 50 per cent. under Fowler's, now rose to 78 and 88; the subjective side was much improved too. The "606" was administered intramuscularly.

Complement Fixation in Leprosy with Leprous Antigen.—R. BIEHLER and J. ELIASBERG (*Deutsche med. Woch.*, 1911, xxxiv, 304) have made studies in complement fixation in leprosy which appear to be of great interest because of the specificity of the reaction. The method of preparing the antigen, which is the important step, is as follows: Fresh lepromes are allowed to autolyze two or three days in a closed vessel at room temperature. The material is then rubbed up with 2 per cent. antiformin solution and placed in a shaker for twenty-four hours. The suspension is now centrifugalized, the supernatant fluid carefully pipetted off and neutralized with 0.1 per cent. normal sulphuric acid. The fluid must be exactly neutral in reaction and is ready for immediate use. The mode of procedure for carrying on the reaction is then given. Sera from 18 cases of leprosy were examined. Of these, 8 were lepra tuberosa, the remaining 10 being lepra nervorum. Antigen such as that described above gave uniform positive results with leprosy sera, and *only* with leprosy sera. Luetic sera were negative when tested with this antigen. Biehler and Eliasberg find that sera from lepra tuberosa find complement more markedly than those from lepra nervorum.

Eosinophilic Intestinal Crises in Sucklings.—L. LANGSTEIN (*Münch. med. Woch.*, 1911, lviii, 623) has previously called attention to the passage of stools consisting largely of mucus and containing many eosinophilic leukocytes in the so-called exudative diathesis of infants. He has had opportunity to observe additional cases since his former report. The mucoid stools, rich in eosinophilic cells, appear in crises which may pass off, with little or no change having been made in the baby's diet. Langstein suggests that the eosinophilic intestinal crises which he has observed may be a kind of "intestinal asthma" (Strümpell) of the suckling. There are no severe general symptoms. Elevation in temperature and change in weight, which would scarcely be lacking in an infectious process, have been conspicuous by their absence.

The Diminished Resistance of Diabetics to Infection.—E. HANDMANN (*Deutsches Archiv f. klin. Med.*, 1911, cii, 1) has investigated the cause of the lowered resistance of diabetics to infections. In the main, he considers, there are two possibilities—one that the lowered resistance is humoral, the other, that it is purely cellular. It is with the former that Handmann has busied himself. As a result of numerous experiments, he has arrived at the following conclusions: (1) Blood containing large quantities of glucose (0.5 to 1 per cent.) is no better medium for the growth of staphylococcus than normal blood. (2) The addition of grape sugar to blood does not lessen its bactericidal power for the staphylococcus, providing the concentration of the glucose be kept within the limits met with in diabetic blood. (3) Similar addition causes no diminution in the normal opsonins of the serum against staphylococcus. (4) The diminished resistance of many diabetics to infections is not, therefore, attributable exclusively, nor even chiefly, to a decrease of the bactericidal properties of the blood or body fluids, but in all probability is to be sought in cellular changes.

The Specific Effect of Salvarsan in Frambœsia.—R. P. STRONG (*Münch. med. Woch.*, 1911, lviii, 398) does not go into the identity or dissimilarity of frambœsia and lues in any detail, but says that the majority of writers at the present time consider the two diseases distinct. Certainly the great resistance of the spirocheta pertenuis to therapeutic measures is more marked than that usually met with in spirocheta pallida. Mercury and arsenic have proved almost useless in the treatment of frambœsia, iodides alone being useful, but not always reliable. In short, the treatment of frambœsia has been extremely unsatisfactory and discouraging. Strong has investigated the action of salvarsan in frambœsia, and finds that it acts as a specific. He has relied mostly on the intragluteal injections of the drug, though a few patients have received it intravenously. The dose was 0.5 to 0.7 gram. The writer has treated 30 cases, and in each there was rapid and striking improvement. The ulcerative lesions, which had been most resistant, healed promptly, and there have been no relapses, though it is now six months since the last patient was treated. The action of salvarsan on the spirocheta pertenuis is therefore specific.

Herpes Zoster and Renal Colic.—A. BITTORF (*Deutsche med. Woch.*, 1911, xxxvii, 290) has been interested in the study of Head's cutaneous zones, and in this connection has had a remarkable case of renal colic. It has been repeatedly observed, in connection with painful diseases of the internal organs that hyperalgesia of the skin, or even herpes zoster, may appear over the cutaneous zone of Head corresponding to the viscus affected. In Bittorf's case of right hydronephrosis with renal colic, a herpes zoster developed in the distribution of the eleventh dorsal segment. (On the other hand, herpes zoster in this region may be associated with pain exactly similar to that observed in renal colic and with marked diminution in, and consequent extremely high color of, the urine, symptoms which have led to an erroneous diagnosis. Such a case was reported several years ago from the clinic of Dieulafoy. (W. S. T.)

Absence of Complement in the Blood of Lepers.—J. ELIASBERG (*Deutsche med. Woch.*, 1911, xxxvii, 302) was the first to note that the serum of lepers is often capable of fixing complement. The cause was not, at first, apparent. The present studies of the writer show, however, that leprous sera are devoid of complement, while possessing antibodies. A somewhat similar state of affairs has been observed in certain syphilitic conditions. In lepers, then, Eliasberg finds that the blood serum contains no complement, but that free amboceptor and antigen are present. Likewise, complement may be lacking in the serum of general paretics, though here amboceptor is again present, and probably antigen, since the latter is demonstrable in the cerebrospinal fluid. It seems probable to Eliasberg that the absence of complement, together with the presence of amboceptor and antigen in the blood of lepers and of progressive paralytics, furnishes the explanation of the incurability of these diseases.

SURGERY.

 UNDER THE CHARGE OF

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Diverticula of the Lower Bowel: Their Development and Relationship to Carcinoma.—WILSON (*Annals of Surgery*, 1911, liii, 223) says that up to the present time 15 cases of diverticula of the lower bowel (1 of the cecum, 12 of the sigmoid, and 2 of the rectum) have been operated on at the Mayo clinic, St. Mary's Hospital. Four of these have proved to be carcinoma apparently arising from diverticula. Of the 15 cases, 9 were males and 6 females. The oldest patient was aged seventy-two years, and the youngest aged forty-one years, with an average of fifty-five years. They were all, therefore, in the cancer period. It is also worthy of note that no clinical case of diverticulitis has been found except in adults. Three of the 15 cases were cases of peridiverticulitis. In these the inflammation did not involve the mucosa. Its presence in the peridiverticular fat was apparently due to leakage through the thin-walled diverticula—a condition similar to that found in old umbilical hernias. Their symptoms were those of peritonitis or obstruction from pressure. In 4 cases carcinoma had developed in the diverticula, probably from epithelium segregated by chronic inflammation.

The Causes of Colon Bacillus Infection of the Urinary Passages.—FRANKE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxii, 542) says that all authorities are agreed that infection of the urine is, in the great majority of cases, due to the colon bacillus. Franke investigated the cases in which urinary infection occurs independently of the passage of instruments into the bladder, and he performed experiments upon dogs. He concluded that there exists a lymphatic connection from the ascending colon, cecum, and appendix, to the right kidney. Whether such an association exists between the corresponding portion of the colon and the left kidney is open to question. Undoubtedly the lymphatics of the descending mesocolon run in front of the left kidney and make an anastomosis here probable. The more frequent occurrence of pyelitis on the right than on the left side, may be explained partly by this lymphatic relation. Bacteria pass easily from the intestine into the lymph vessels when there is slight disturbance of the intestinal function. When the bladder is found infected and the kidneys free, the infection may still have found entrance by way of the kidney.

On the Coincidence of Volvulus and Real or Simulated Strangulated Hernia.—MILLER (*Annals of Surgery*, 1911, liii, 232) says that volvulus may produce in a hernia signs and symptoms which accurately simulate hernial strangulation; or it may be associated with actual strangulated hernia. In either case it may escape recognition; it is probably contributing heavily to the mortality of strangulated hernia. The diagnosis before operation is exceedingly difficult; there are, however, certain very suggestive features, viz., advanced age, the presence of a hernia for many years, shock out of proportion to the signs about the rupture, and marked abdominal pain and tenderness with occasionally a palpable mass. The diagnosis at operation depends upon careful observation, there being certain signs which are pathognomonic; an operation undertaken for strangulated hernia must demonstrate absolutely the strangulation. Volvulus proximal to actual strangulated hernia apparently offers no sure means of diagnosis other than routine abdominal exploration—a procedure which is manifestly not to be recommended.

Further Observations Concerning the Value and Importance of Leukocytosis and the Neutrophile Blood Picture in Appendicitis.—KOHLE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxii, 542) says that for the determination of the neutrophilic blood picture it suffices for practical purposes to take account only of the mononuclears, and to represent them in the form of a curve. The leukocyte counts should be followed in a similar manner. The leukocytes should be counted in every case of acute appendicitis, whether operation is done or not. It is only the total blood picture that is of value, but this is of at least as much value as the temperature and pulse curve. When the latter do not agree with the remaining clinical symptoms the blood picture will decide the question. In general the blood picture is an expression of the virulence of the infection, while the leukocytosis corresponds to the degree of peritoneal irritation and the capacity of the individual for reaction. Increased leukocytosis with a normal or nearly normal blood picture gives a good prognosis. The higher the blood picture mounts, the more severe the infection and the more serious the prognosis. If the leukocytosis is increased, it is a favorable sign (good resistance), while a low leukocytosis with a high blood picture is always a serious sign. A simultaneous moderate increase of the curves is a favorable sign, as is an increase of one or the other curves or an intersection of the curves. The most unfavorable cases are those of peritonitis, with a very high blood picture curve and a normal or subnormal leukocytosis. If after operation the blood picture curve is low and the leukocytosis high, the tendency is to improvement, the organism gaining the upper hand in the fight against the infection. One observes at times, after an operation, a high mounting of the blood pictures, possibly with a sinking of the leukocytosis and soon after a return of the curve to the normal. This postoperative rise, probably due to a stirring up of an encapsulated focus of inflammation, does not affect the prognosis. A slow, steady rise of the blood picture, probably after a brief decrease, is a very serious sign, since it indicates an advance of the infection. Abscesses (primary and secondary) are indicated by increase of the leukocytosis, while the temperature and pulse at times may be normal. If the leukocytosis is low before the opening of the abscess,

it indicates an encapsulation of the abscess. With the increase of the leukocytosis the blood picture usually increases, according to the grade of the infection. One should refrain from early operation only in such cases as give mild clinical symptoms, especially a slight local tenderness and a normal or slightly increased blood picture and leukocytosis. If, however, this is a recurrent attack, immediate operation should be done. If the clinical symptoms are mild and the leukocytosis high, operation should be done. A low leukocytosis and a normal blood picture do not contraindicate operation when the clinical symptoms are severe, especially if there is marked local tenderness. In these cases there is usually a retrocecal inflammation, often extraperitoneal and limited to the appendiceal region.

A Contribution to the Appendicitis Question Based upon the Operations Performed in the Göttingen Clinic in the Last Fourteen Years.—FROMME (*Deut. Zschr. f. Chir.*, 1911, cviii, 429) says that during this period 647 patients with appendicitis were treated, 390 men and 247 women. Of these, 46 men and 13 women died; the men suffering more frequently from the severe forms of the disease. Fromme believes that the best method of treatment of acute appendicitis is early operation. It should be recommended in every case in which the symptoms are at all acute, since a positive prognosis is not possible at the present time and only by early operation can the severe forms of the disease, especially abscess and peritonitis, be avoided. In the intermediate stage, say from the third to the fifth day, operation should be delayed until a distinct abscess is formed or the interval stage has developed. This will decrease the number of cases in which operation becomes imperative to save life, and in such cases as diffuse peritonitis the appendix should be removed. In opening an abscess in the late stages it is not necessary to remove the appendix, but it is sufficient to make a small incision to evacuate pus. By suturing the abdominal wall down to and around the drainable tube and gauze a hernia will almost certainly be avoided. Abscess operations need not be delayed until the interval, but should be done during the early symptoms, in the first days. Cases without abscess recur frequently, and should be operated on in the interval. The interval operation should be performed after mild attacks as soon as the symptoms disappear; after severe attacks, in from four to six weeks. Peritonitis should always be operated on and the appendix removed. The abdominal incision should be sutured around the drainage tube and gauze. The irrigation methods of treatment, where there is a free exudate, denote an advance over the earlier methods.

Opening up a New Pathway for the Return Circulation in Obstructive Changes in the Abdomen and Lower Extremities.—LANZ (*Deut. Zschr. f. Chir.*, 1911, xxxviii, 153) says that he has performed Talma's operation for an obstructed portal circulation in 4 cases, with good results in 2, while in the other 2 they were completely negative. He reports the case of a man, aged sixty-nine years, who was admitted to the clinic with a diagnosis of hepatic cirrhosis, which was based upon the presence of marked ascites and a history of alcoholism. An examination of the liver was prevented by the enormous distention and filling of the abdo-

men. There was no oedema. The urine was normal and the lungs were free. The absence of dilated veins under the skin of the abdomen was striking, and in view of the age of the patient a clinical diagnosis of peritonitis carcinomatosa was made, although neither a tumor nor intestinal obstruction was evident. Under local anesthesia an incision was made in the right inguinal region as for an inguinal hernia. The peritoneum was punctured with a knife and from 12 to 15 liters of yellowish ascitic fluid escaped. The peritoneum was then widely opened and found covered with miliary, grayish-white, hard nodules, which appeared to be carcinomatous in nature. The right testicle was pulled upward by the spermatic cord and freed from the fundus of the serotum by crushing the gubernacula with a Roux's angiotribe. The tunica vaginalis was then incised and the testicle brought into the free peritoneal cavity. The spermatic cord was then sutured in its whole length to both sides of the peritoneal incision. The peritoneum was closed by a continuous suture, the lowest muscle sutured to Poupart's ligament, and the opening in the external oblique aponeurosis also closed. A continuous skin suture was introduced and a collodion dressing applied. The patient made a good recovery. There was no recurrence of the abdominal effusion and the general condition improved. The patient died, however, five weeks after operation. Microscopic examination of the nodule showed it to be tuberculous.

Concerning Bilateral Empyema.—FABRIKANT (*Deut. Zschr. f. Chir.*, 1911, cviii, 584) says that as a result of his experience with one case of bilateral empyema, operated on in 1897, he concerned himself with several questions which have not been satisfactorily answered by writers on this subject. They were as follows: May one operate on both sides simultaneously without fear of a double pneumothorax, and with the hope that pleural adhesions will prevent collapse of the lungs? How shall one proceed, if for caution's sake he wishes to operate on only one side and the condition of the patient requires that the pus should be evacuated from the other side also? May one be satisfied with aspiration on both sides or with aspiration on one side and a radical operation on the other? As a result of his study he concludes that bilateral empyema occurs most frequently in children, and much more rarely after thirty years of age. From the etiological standpoint the most frequent cause is a unilateral or bilateral pneumonia, although primary empyema can occur. The mortality from the operative treatment of bilateral empyema is not high when operation is performed at the proper stage. One may operate on both sides at the same time when the condition of the patient requires it. It is better, however, to permit an interval of a few days to pass by between the two operations. The bilateral pneumothorax is not dangerous. Therefore it is better to open both sides, rather than open one side and be satisfied with aspiration on the other. Puncture and aspiration cannot replace the free opening on both sides. Whether or not one should perform rib resection or thoracotomy will depend upon the width of the intercostal spaces. If they are wide thoracotomy will suffice. The operation will be performed easily without pain under local anesthesia. Since displacement of the heart was not present in Fabrikant's case, the paralysis of the vocal cords which was present cannot be explained by mechanical

traction on the recurrent laryngeal nerve. It is rather to be explained by compression of the nerves and veins by the pleura thickened by cedema.

An Operation for Exstrophy of the Bladder, with Provision for the Ureters After Extirpation of the Bladder.—SPANNAUS (*Zentralbl. f. Chir.*, 1911, xxxviii, 225) employed the lowest loop of the ileum as a reservoir for the urine, because the backflow of feces from the colon was prevented by the ileocecal valve. This was first proved by operations on dogs. To diminish shock the operation was divided into two stages. In the first, after dividing the ileum an anastomosis was made between the proximal end of the ileum and the transverse colon, thus isolating the lowest portion of the ileum, which was to be employed as the urinary reservoir. In the second operation the bladder was extirpated and the ureters implanted into the isolated piece of ileum. To prevent peritonitis this portion of ileum was placed in the extraperitoneal position previously occupied by the bladder. This prevented the necessity of displacing the ureters, and therefore their kinking. In dogs it was found impossible to observe the results of the operation more than a few days, since, notwithstanding the two-stage operation, the dogs died. Spannaus had the opportunity of performing a modification of the operation on two cases. In the first, a man, aged forty-three years, the whole bladder, filled with a recurring papilloma which bled continuously, was extirpated. In the first stage the lowest loop of ileum was excluded and an anastomosis made between the proximal end of the ileum and the transverse colon. In the second stage the bladder was removed and the ureters implanted into the isolated ileum, now placed extraperitoneally. Drainage through the urethra and from above. On the third day the bowels were removed and showed a fluid mass with the odor of urine. In the following days the stools occurred every two hours, but from the sixth day on they diminished in frequency. On the tenth day urine passed through the catheter. Six weeks after operation the patient died. In a second patient a similar operation was performed, but the patient died on the seventh day. It is concluded that the passage of the urine through the whole of the large intestine is dangerous, because of the damage done to the mucous membrane and the absorption of the poisonous constituents of the urine.

Röntgenological Examinations of the Kidney.—HOLDING (*Amer. Jour. Urology*, 1911, vii, 18) says that large experience has demonstrated certain dicta in regard to Röntgenological examinations of the urinary tract. Among them are the following: A positive diagnosis of calculus should only be made after the entire urinary tract has been radiographed and the shadow of the lesion has been duplicated in at least two radiographs. A negative diagnosis is only justified when the outlines of the transverse processes of the vertebræ, the psoas muscle, and the kidney are shown. It is not always possible to show these details in very large patients or in those whose bowels have not been properly prepared previous to the examination. The correct interpretation is very important. Pseudocalculus shadows may be caused by many substances introduced into the body, as Bland or silver pills, and conditions existing in the body, as the calcification of cartilages,

phleboliths, etc. Sometimes they cannot be explained except by autopsy. On the other hand, skilful surgeons have failed to find stones at operation, when a positive radiographic diagnosis has been made and the patients have later passed stones corresponding in number, size, and shape to the shadows obtained on the radiographic plates. In selected cases it will be found to be an advantage to check the x-ray findings by cystoscopy and ureteral catheterization. To verify a diagnosis of pseudocalculus it may be necessary to demonstrate the path of the ureter by catheterizing the ureter, using a bismuth ureteral catheter and radiographing with it *in situ*. The symptoms of a calculus of the kidney may be on one side when the calculus is in the kidney on the other side of the patient (Renorenal reflex). Most patients having typical attacks of renal colic do not have calculi, and, on the other hand, only very few of the patients who have calculi have symptoms sufficiently characteristic to justify an operation. As a preliminary the bowels should be properly prepared over a course of at least one, and in some cases two or three days preceding the examinations. To make a diagnosis of calculus from a plate made without such a preliminary preparation is dangerous. Characteristic symptoms of nephrolithiasis have presented in cases which proved to be cholecystitis; renal tuberculosis; renal cancer; hypernephroma; pyelitis; empyema of the renal pelvis; bacilluria; hydronephrosis; cystic kidney; prostatic disease or calculi; seminal vesiculitis; diseases of the urinary bladder; essential hematuria, or that associated with scurvy, purpura, or leukemia; chronic appendicitis; diseases of the spine, especially osteo-arthritis or Pott's disease in the adult; muscular rheumatism, with spasm of the muscles of the back; flatulence. In women the passing of wax-tipped catheters may give valuable information, but this method is not of as much value in men because of structural differences necessary in the male cystoscope. The absence of pain and danger of infection in making radiographic examinations, and the information gained as to the positive size and surfaces of stones (whether rough or smooth, therefore, whether movable or not), and the number of calculi present, make the radiographic method the one of preference; to be supplemented by other methods if necessary. The larger the calculus, the less typical are the symptoms; the small calculi give the most typical attacks of colic. Other diseases of the kidneys that can be demonstrated by radiographs are nephroptosis, tumors, hydronephrosis, pyonephrosis, and ureteral anomalies.

THERAPEUTICS.

UNDER THE CHARGE OF

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Salvarsan Treatment: Retrospect and Outlook.—*EHRLICH (Münch. med. Woch., 1911, lviii, 1)* answers many of the objections that have arisen with regard to salvarsan. He believes that many of these objections

can be explained by failure to follow his explicit instructions, and consequently failure resulted. Furthermore, he has never promised that a single dose of the remedy would be curative. Ehrlich says that from the first he has given as contraindications for salvarsan treatment those patients with irritable hearts due to nervous causes, organic heart disease, vascular degenerations, aneurysms, old cases of cerebral hemorrhage, and the aged. He now adds to this list the following: Serious nephritis, diabetes, and ulcer of the stomach. He does not consider the remedy a harmless one, but one that should be used with caution in properly selected cases. With regard to fatalities, he compares it to chloroform, saying that in healthy individuals there is 1 death in 50,000 anesthetizations, while in hospital practice this rate rises to 1 in 2070. He explains the few bladder disturbances that have been reported by an oxidation of the remedy because of defective bottles. He mentions the cases reported by Benario and others, of optic and auditory nerve affections following salvarsan injections, and relates similar recurrences in the nervous system that have been observed after mercurial treatment. He says that the fact that many of these were cured by subsequent injections of salvarsan, speaks emphatically against their toxic origin. Ehrlich repeats the warning that salvarsan should not be given to a patient who has had other arsenical treatment. To this fact of previous arsenical treatment he attributes the optic neuritis of a case of Finger. Ehrlich says that the best effects of salvarsan are seen in syphilitic mouth and throat affections, those of the nasal mucous membrane, secondary and tertiary skin manifestations, malignant syphilis, congenital syphilis, and those cases that do not yield to mercury. Ehrlich believes that, although he may not have attained his ideal of a *therapia sterilisans magna*, still this remedy is an advance upon the former treatment, and he may in the future discover the ideal remedy.

Dehydration by Dietetic Measures.—MAGNUS-LEVY (*Jour. Amer. Med. Assoc.*, 1910, lv, 2139) says that the dietetic treatment of circulatory diseases is essentially a form of protective therapy, a term that is better expressed by the German word *Schonungstherapie*. He discusses especially the methods of treatment as applied by Karel, Oertel, and Widal. The essential feature of the Karel treatment is the exclusive use of milk in relatively small quantities at definitely stated intervals. The idea underlying Oertel's method is a great reduction in the quantity of fluid ingested. The Widal treatment, on the other hand, consists in excluding sodium chloride as much as possible from the food, which in other respects is the ordinary mixed diet. Magnus-Levy discusses the theories and the methods of application of these different plans of treatment. He compares the different methods and points out their differences and similarities. The Widal treatment has a low sodium chloride content in common with the strict milk cure of Karel, but differs from that of Widal in the great reduction in the amount of all foodstuffs. The ordinary salt-poor diet as advocated by Widal contains only from 1.5 to 2 grams of salt, while 3 liters of milk, which is the minimum amount necessary to maintain equilibrium, contain 5 grams of sodium chloride. The method of Karel reduces the amount of all the foodstuffs. During the first week the patient does not receive

even a fifth of his requirements, and during the first five or six weeks the physiological minimum is never reached. In many cases the Karell treatment is more suitable than that of Widal, but has the disadvantage that the patient loses considerably in body protein and fat. Magnus-Levy says that the ingestion of all organic foodstuffs increases the amount of fluid in the body in a manner similar to sodium chloride, though not to quite so marked a degree and by a somewhat different mechanism. Fat appears to do this least. The absorption of the carbohydrates demands considerable water since the glucose content of the blood serum rises only from 0.1 to 0.3 per cent. at the most. On the other hand, the water metabolism is most strongly influenced by the protein molecule. Not only does it require for its absorption and its transportation relatively large amounts of water, but its end-products also demand considerable amounts of fluids for their excretion. Thus, Oertel's two principles of low water and high protein intake—he required up to 200 grams of protein a day—are at variance with each other. The relationship of the protein metabolism and of sodium chloride to the water metabolism is particularly well shown in diabetes insipidus. In the true forms of this affection it is impossible to control the increased excretion of urine by applying Oertel's treatment, but thirst and the amount of urine excreted immediately become less when the amount of salt intake is reduced. The same result is obtained by reducing the protein intake. In a similar way the reduction of the amount of protein in the food is of benefit in all circulatory disorders, although the effect is not so noticeable as in diabetes insipidus. In discussing these three methods of reducing the amount of body fluids, Magnus-Levy says that the effect of reducing the water intake (Oertel's treatment) was especially marked in such cases where a great excess of water had previously been taken. He believes that the reduction of the amount of fluid ingested also acts indirectly by inducing the patient to become unconsciously more abstemious in eating, and usually to avoid strongly salted food which increases thirst. The reduction of sodium chloride (the method of Widal) is indicated especially in the oedema of parenchymatous nephritis, but is also useful in combating some of the symptoms of contracted kidney, such as headache, uremic asthma, angina pectoris, and pulmonary oedema. This treatment also has been valuable for diabetes insipidus and cirrhosis of the liver. Patients who have improved after such a diet should not return to their ordinary salty diet, although the excretory capacity for salt may undergo a considerable improvement. He suggests giving the patient accurately weighed quantities of salt which he may add to his food up to his individual limit of tolerance. Patients with diabetes insipidus must permanently refrain from a salty diet, since it is impossible to improve the capacity of the diseased kidney for excreting concentrated urine. The writer ascribes some of the benefits of the Karell method to the restricted protein intake. In addition to its immediate effect upon water metabolism a low protein diet probably acts favorably in other ways. Such a diet is particularly to be recommended in those cardiac patients who were previously high liverers and exhibit a certain degree of plethora. It is also indicated in the later stages of chronic interstitial nephritis with uremic manifestations. Magnus-Levy says that these treatments should be carried out exactly according to the direction

of Karel, Oertel and Widai, in order to overcome certain difficulties in their application. When this has been done a few times it will be easier to modify these treatments to suit individual cases.

The Administration of Salvarsan.—MONTGOMERY (*Jour. Amer. Med. Assoc.*, 1911, lvi, 501) discusses in brief the remedy and the preparation of the solutions for intramuscular and subcutaneous use. He prefers the administration of salvarsan by intravenous injection since the remedy is given in a painless manner that insures the rapid diffusion of the full dose without running the risk of ensuing necrosis or abscesses, or of chronic arsenical poisoning from prolonged absorption. Montgomery gives a very clear and detailed description of the technique of the intravenous administration as practised by Schreiber. About 20 c.c. of warm distilled water are poured into a graduated glass cylinder of a capacity of 250 c.c. This cylinder should have a glass stopper. The glass capsule containing the salvarsan powder is now wiped off with gauze soaked in alcohol, and then with gauze soaked in ether. After breaking the capsule, the powder is poured on the water in the graduated glass tube, the stopper put in, and the contents well shaken. There is no necessity of using glass balls here, as the quantity of water is ample to dissolve the salvarsan readily. It is important not to reverse this procedure, for if the powder is poured into the tube first, and the water afterward, a gummy mass forms in the bottom that dissolves with difficulty. This solution should be light yellow and perfectly clear. That it should be clear is a matter of very great importance, as it is highly necessary that no undissolved particles be present. Now we have an acid solution in sterilized water of the contents of one tube, the quantity of which is usually 0.5 or 0.6 gram. If it is 0.5, the graduated tube should be filled up with water to the 50 c.c. mark; if 0.6, to the 60 c.c. mark, so that each 10 c.c. will represent 0.1 of the drug. Schreiber usually gives 0.3 gram of salvarsan to a woman and 0.4 gram to a man. If it is desired to give 0.4, he pours 40 c.c. of the acid solution into another graduate furnished with a glass stopper, and fills up to the 200 c.c. mark with warm sterilized water, and to this adds about 20 c.c. of normal sodium hydroxide solution. This should be added a little at a time, and each time a little is added the glass stopper should be put in and the cylinder well shaken. At first a precipitate forms that gradually disappears on the addition of more caustic soda solution. When the solution is again clear, it is alkaline and ready for injection. The flask containing the sterilized distilled water for use in making the solutions should not be stoppered with cotton, but with gauze, as cotton fibers, falling into the fluid, might cause trouble. The best syringe for injecting is a glass Luer of about 20 c.c. capacity. It should not have a metal plunger, as in that case the least blood may cause binding. A two-way cock is introduced between the needle and the barrel. Schreiber has a special needle made with a bayonet bend in the shaft, and on this bend a ribbed finger-hold. The bayonet bend is to allow the needle to be more easily shoved along in the lumen of the vein. A rubber tube is fitted to the lateral outlet of the two-way cock. The arm is now laid out on a cushion, so as to lie flat and easy; a stout rubber tube is thrown around the middle of the upper arm and drawn tight enough to stop the flow of blood in the superficial veins, but not

so tight as to impede the arterial supply, and fastened with artery forceps or a modern clip. It is very necessary that the arm should lie easy and still. The seat of operation should be wiped off with gauze soaked in alcohol. About 4 c.c. of normal salt solution are drawn into the syringe, so that by running the plunger forward the air may be expelled from the needle and from the rubber tube attached to the outlets of the two-way cock. The needle is then inserted through the skin over a vein, and run along into the vein. When the needle enters the vein a little blood flows back into the normal salt solution in the syringe. If the plunger is pressed forward, the salt solution entering the vein will distend it a little, and when it does so the tourniquet band about the arm may be removed, and the vein will collapse. The insertion of the needle is a very important step in the operation. For instance, by blood flowing back into the syringe it is known that the needle has entered the vein. The syringe, still containing a little salt solution and with its needle lying in the vein, is now ready for injecting the fluid, which is held in a glass beaker so that the rubber tube attached to the lateral opening of the two-way tap drops into it. The instrument is free of air, so that there is no fear of air embolus. By turning the cock of the two-way tap, the salvarsan solution may be alternately sucked up into the syringe, and forced into the vein. When the salvarsan solution is almost exhausted, a little normal salt solution is thrown into the beaker, and also injected into the vein. This is to clear away any of the salvarsan solution that would otherwise trickle out into the tissues, on withdrawing the needle. A very important matter in this part of the operation is the injection of the small quantity of normal salt solution, both before and after injecting the salvarsan. By injecting the normal salt solution at first one makes sure that the needle is in the vein, for if it is not in the vein, the injected fluid makes a little infiltration in the subcutaneous tissue, while if it is in its proper position the already distended vein grows a little larger. If this sign should fail there is still a symptom showing that the needle is not in place, for as soon as a little of the salvarsan enters the subcutaneous tissue the patient will experience a burning pain, in which case the needle should be immediately withdrawn and free bleeding induced from the punctured wound. Another vein should then be chosen for the injection. Any subcutaneous vein that can be distended may be chosen, and in fleshy women Schreiber has even injected into one at the wrist. Sometimes when the vein cannot be seen it may be felt. The fluid should be injected slowly, say in five or six minutes, so as to avoid sudden overloading of the circulatory system. Although the description of the operation is long, tedious, and complicated, yet the performance is very simple, and the patients experience very little inconvenience. They should remain twenty-four hours in bed.

Treatment of Splenic Anemia by Splenectomy.—SUTHERLAND and BURGHARD (*Lancet*, 1910, clxxix, 1819) report 2 cases of splenic anemia successfully treated by splenectomy. They give the details of the cases treated. One patient, a girl, aged twelve years, was in very bad condition when operated on. Three days after the operation the red cells had increased from 2,500,000 to 4,700,000, and the hemoglobin from 40 per cent. to 76 per cent. This change was accompanied by a marked

difference in the appearance of the child. Four years after the operation a blood examination showed a hemoglobin percentage of 78 per cent. and a red blood count of 3,600,000. The second patient was a girl, aged six years. Four days after the operation the red cells increased from 1,870,000 to 4,000,000, hemoglobin from 30 per cent. to 52 per cent., and leukocytes from 2400 to 10,800. Nucleated forms of red blood cells that were previously abundant had disappeared from the blood, as did also degenerated forms of red blood cells. In the count previous to operation there were 1.2 per cent. of myelocytes present and degenerated forms of leukocytes. These also disappeared after the operation. On the seventeenth day after the operation the red cells were 5,200,000; white cells, 3400, and the hemoglobin was 65 per cent. Seven weeks after the operation the patient was practically well.

PEDIATRICS.

UNDER THE CHARGE OF

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Investigation on Tuberculous Infection in Children.—ROTHE (*Deutsch. med. Woch.*, 1911, xxxvii, 343) has instituted investigations supplementing those made by Gaffky, in order to determine the frequency of bronchial and mesenteric tuberculosis in children—the mode of invasion, and the significance of bovine tuberculosis in this connection. The Gaffky series of 300 cases coming to autopsy showed, by animal experimentation, 19 per cent. infected with tuberculosis; glandular infection was proved in 29 cases, 11 in the mesenteric, and 17 in the bronchial glands. In 55 cases 78 pure cultures were obtained, all belonging to the human type of tuberculosis. Rothe's material was obtained from 100 autopsies on children up to the fifth year. The bronchial and mesenteric glands in each case were tested by injection into guinea-pigs—264 guinea-pigs with mesenteric, 250 with bronchial glandular material. The positive strains were worked out through subsequent injections on guinea-pigs and rabbits. Out of the 100 cases investigated, 77 were under two years of age. In the 55 males, 27.27 per cent. were proved tuberculous. Of the 45 females, only 13.33 per cent. proved positive. The total positive percentage in the series was 21 per cent. In 13 of these 21 cases, both the bronchial and mesenteric glands were infected; in 3 cases the mesenteric glands alone, and in 5 cases the bronchial glands alone, were infected. This tends to show that the infection does not, as a rule, occur through the intestinal tract. From the 34 pure cultures obtained, 32 belonged to the human type and only 2 to the bovine type. Combining Gaffky's and Rothe's series, making a total of 400 cases, 20 per cent. were proved tuberculous. Both sets of glands were infected in 42 cases, 14 times in the mesenteric and 22 times in the bronchial glands, showing that the intestinal tract as an entrance is not a strong factor in children, and that the respira-

tory tract is the usual entrance of the infection. Taking into consideration only those cases in which a pure culture was obtained, it was found that out of 76 tuberculous cases, 75, or 98.68 per cent., were of the human type, and 1, or 1.32 per cent., was of the bovine type of tuberculosis. Two other cases of presumably the bovine type were discovered. The investigation supports the statement of R. Koch that the danger in childhood from the bovine type of the disease fades into insignificance in comparison to the danger from the human type of bacillus.

Venous Murmurs Heard at the Root of the Neck in Children.—CAREY COOMBS (*Brit. Jour. Child. Dis.*, 1911, viii, 109) has investigated the venous hum in children described by Eustace Smith as a sign of tuberculosis of the mediastinal lymph glands. One hundred connective cases were studied, ranging from one to fifteen years of age. Out of this number, 51 exhibited the murmur. The murmur occurred twenty-six times in 42 boys, and twenty-five times in 58 girls; 50 per cent. of the murmurs were found in children under two years, 58 per cent. from two to five years, 76.6 per cent. from six to ten years; and 50 per cent. from eleven to fifteen years. Excepting in a few cases of anemia it is unusual to find this murmur in persons over sixteen years old. The murmur is heard at and just below the sternoclavicular articulations. The following facts were demonstrated: If bilateral, the murmur is louder on the right side. If unilateral, it is more often on the right side. With the head thrown back the murmur becomes more audible and lateral rotation has the same effect. The murmur usually disappears in the recumbent position. It is usually louder during inspiration, and louder during cardiac diastole more often than during systole, but it is accentuated at the beginning of each phase. It is low-pitched, usually, and reminiscent of the chlorotic "bruit de diable." The murmur is not especially associated with tuberculous adenitis within the thorax, as shown by its presence fifty-one times in 100 non-tuberculous children, its presence in many children who have never been ill, and its absence in a number of cases with intrathoracic tuberculous glands. It cannot be regarded as a sign of any gross organic change. Probably in some cases of fever and anemia the murmur may appear as do bruits at the cardiac base. The murmur is certainly venous and is heard over the internal jugular veins in the neck and over the innominate veins beneath the manubrium. It is produced in the internal jugular vein, but the mechanism is not clear. Although associated with anemias and febrile states, it is heard also in perfectly healthy children. It is not associated with tuberculosis, and is of no diagnostic value.

The Difference Between the Manifestations of Rheumatism in Childhood and Adult Life.—J. BOYD BARRETT (*Brit. Jour. Child. Dis.*, 1911, viii, 113) points out that rheumatism in childhood differs from the adult form in the variety of its manifestations, in its insidious onset, in the mildness of its arthritic symptoms, and in the severity of the cardiac conditions. Its manifestations in children are given as myocarditis, endocarditis, pericarditis, rheumatic nodules, muscular rheumatism, erythematous eruptions, chorea, pleurisy, and tonsillitis. Hyperpyrexia and acute polyarthritides are rarely found in childhood,

being associated with the adult form. The mild arthritic and the mild primary form with endocarditis are the most important to recognize in children, to avoid irreparable injury. Wasting is one of the effects of advanced cardiac disease subsequent to rheumatic endocarditis, often without a history of joint inflammation. Anemia is a complication more frequent in children than in adults. Rheumatic nodules are associated with and diagnostic of the disease in children. They are often found in young adults, occurring on the ears. They are almond-shaped, hard and freely movable, and occur beneath the skin over bony points, such as the olecranon and patella. Their structure is fibrous, the fibers being arranged concentrically. They are associated with endocarditis. In rheumatic tonsillitis the diagnosis is often provisional. Tonsillitis is occasionally followed by arthritis and rather often by endocarditis and pericarditis. Wachenheim gives 60 per cent. of cases with cardiac lesions out of 113 cases of rheumatism in children. McCrae gives 3.7 per cent. of cases of rheumatism, showing tonsillitis, and Hamerschmidt gives 50 per cent. Preponderance of opinion favors the association of chorea with rheumatism, and this makes a further difference between the child and the adult. In cardiac rheumatism, the earliest phenomena is usually an acute dilatation of the left ventricle, a diffuse or weakened cardiac impulse, a feeble first sound at the apex, and an accentuation of the pulmonic and sometimes the aortic second sound. Clinical experience shows that the acute dilatation of the left ventricle is present in even mild attacks of subacute rheumatism. The treatment includes early and prolonged rest in bed, and full doses of the salicylates with bicarbonate of soda. The administration of digitalis is an important part of the treatment. Rheumatism in any form is rare under two or three years. It is most frequent between six and nine years.

The Value of Lumbar Puncture and the Leukocyte Count in Infantile Paralysis.—JOHN LOVETT MORSE (*Archives of Pediat.*, 1911, xxviii, 164) reviews the results of lumbar punctures in this disease by various investigators. From these data he concludes that during the acute stage of this disease the cerebrospinal fluid is clear and occasionally under pressure; that a fibrin clot is often present, which may persist for several weeks; that the fluid always contains an excess of cells, chiefly of the mononuclear type, most of them being lymphocytes; and that these changes are present before the appearance of the paralysis. These changes, however, are identical with those found in tuberculous meningitis. In the latter case, it is true, the cerebrospinal fluid contains the tubercle bacilli, but these are missed in the majority of cases under the usual routine examination. If they are not found, the examination of the fluid is of no value in a differential diagnosis. Lumbar puncture is of great value in differentiating early anterior poliomyelitis from early cerebrospinal meningitis, as the characteristics are so different in the two diseases—in the latter the fluid being turbid or purulent, and containing many polynuclear cells and often meningococci. The value of lumbar puncture in the early diagnosis of anterior poliomyelitis is very limited. The results of the leukocyte counts in this disease have not been uniform. Morse quotes the leukocyte counts taken in 9 cases. There was never a diminution of the white

cells, but usually a moderate or marked leukocytosis. The most marked leukocytosis occurred on the day on which paralysis appeared. At present, therefore, the conclusion must be reached that the leukocyte count is of little or no assistance in the early diagnosis of anterior poliomyelitis. The evidence at present is insufficient to show whether there is a relative or absolute lymphocytosis in the early stages. If this be proved to be a fairly constant phenomenon, it should be of considerable assistance in early diagnosis.

OBSTETRICS.

UNDER THE CHARGE OF

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The Anaphylactic Theory of the Toxemia of Pregnancy.—JOHNSTONE (*Journal of Obstetrics and Gynecology of the British Empire*, February, 1911) draws attention to the fact that certain organic substances of complex proteins, when introduced for the first time into an organism in subtoxic or non-toxic doses, have the property of producing after a certain fixed incubation period, an excessive sensitiveness to subsequent very small doses of the same substance. If a rabbit be injected with 5 c.c. of horse serum, after ten days the rabbit is profoundly affected by a very small second dose of the same serum. The symptoms produced come on almost at once—blanching of the ears, dyspnea, palpitation, loss of muscular tone, and in severe cases, convulsions, paralysis, and death. This is thought to be due to the development of certain properties in the blood serum; and this supersensitiveness can be transferred to another animal of the same species by the injection of serum from a supersensitized animal. It is thought that the protein first injected acts as an antigen, causing the formation in the blood of an antibody called “anaphylactic reaction body,” which requires a certain fixed time for its formation. At the second injection this body unites with the antigen, probably in the nerve cells, causing shock. The reaction is probably a specific one, as immunity is specific. Johnstone experimented upon rabbits with an extract of healthy human placenta, and also the extract of toxic placenta. He found that anaphylactic symptoms were obtained by the use of normal human placental juice in 8 out of 12 rabbits, indicating that human placental juice contained some complex protein probably capable of acting as a toxin for other animals. When extract of eclamptic placenta was used, no results followed, as the toxic element had probably passed out of the placenta into the patient's body. No results followed the use of extracts from animals of the same species. Powdered placenta was inert. The result of his experiments supports the view that there is no evidence of anaphylaxis in the commoner manifestations of the toxemia of pregnancy.

Cesarean Section in Non-contracted Pelvis.—SIMPSON (*Journal of Obstetrics and Gynecology of the British Empire*, February, 1911) reports 3 cases of Cesarean section in non-contracted pelvis. The first was that of a primipara whose pregnant condition was complicated by a pelvic tumor which obstructed delivery. The patient was operated upon about two weeks before term, as she had sharp pain in the lower portion of the abdomen, and a temperature over 100° F. She was delivered by Cesarean section and a large ovarian cyst afterward removed. The cyst contained semipurulent fluid from infection with the *Bacillus coli communis*. The second case was that of a primipara in labor, the head being pushed aside by a boggy, soft, oval swelling below and to the right of the cervix. Under anesthesia an effort was made to push the tumor out of the pelvis to allow the head to engage. This was found impossible. The child was delivered by Cesarean section, and the cause of obstruction found to be a second uterus about three and one-half inches long, and with it a rudimentary third ovary and tube. These were removed. Subsequent examination showed a small opening to the right of the vagina communicating with a second complete vagina, at the top of which was a small cervix. The patient gave no history of menstrual irregularity, and menstruation ceased during pregnancy. The third case was that of a primipara over forty years of age, who three weeks before term had a slight hemorrhagic discharge without pain. After getting up out of bed the patient had a sharp hemorrhage without pain, and on examination the cervix was very hard, admitting only the tip of the finger. There was marked pulsation in the vaginal vault, and apparently something soft between the fetal head and the lower uterine segment. A firm tampon of gauze was inserted and the hemorrhage ceased. About thirty-six hours afterward another considerable hemorrhage occurred, and on examining the patient under an anesthetic, the finger was introduced, finding a central placenta prævia. The patient was then delivered by section of a living child. In the 3 cases the mothers and children made good recoveries.

Scopolamin in Obstetric Anesthesia.—LEQUEx (*L'Obstetrique*, February, 1911) contributes an extensive paper upon this subject. He quotes the results obtained by 31 different observers, aggregating several thousand cases. In analyzing the reports of these writers, opinions differ as to the value of this drug in producing obstetric anesthesia. Steinbuchel, Krönig, Gauss, and Weingarten, have had good results from the use of this remedy in diminishing the pain of labor, without affecting the consciousness of the patient, making the labor pains less severe and more regular, without decreasing the contracting power of the uterus. They observed no effect upon the fetus. Others admit the advantage of scopolamine-morphine for the mother, but believe it may produce bad results upon the child, which should be attributed to the morphine. Others, among whom is Newell, believe the method dangerous in inexperienced hands or when the solution has become partially decomposed. Beruti had one fatal case among 600 mothers and the deaths of 11 children. Hocheisen believes the drug poisonous to both mother and child.

Multiple Cesarean Section.—McPHERSON (*Amer. Jour. of Obstet.*, March, 1911) gives the results of 39 multiple Cesarean sections. Of these, 30 were done for the second delivery; 7 for the third; and 1 for the fourth and fifth. In 18 cases no adhesions were found; in 11 very few; in 7 many; in 1 the uterus was adherent to the abdominal wall; and in 2 cases no note regarding adhesions was made; in 9 cases no scar could be found in the uterus of former operations. The uterus was found thinner than normal in 25; very thin in 4; and ruptured in 1 case in which many adhesions were present. Among these patients three mothers died, one from anesthesia before the uterus was opened; the second from sepsis on the third day; the third from pneumonia on the fifth day. Where the operation is carefully performed there is no reason why the patient should not be delivered in this manner of several children, with abundant time between the operations for a thorough recovery.

One Hundred and Sixty-one Cases of Eclampsia.—ALBECK (*Ztschr. f. Geburts. und Gynäk.*, 1910, lxxvii, Heft 1) reports 161 cases of eclampsia in Meyer's clinic in Copenhagen. The pathological study of these cases revealed nothing to which attention has not already been brought by others. The phenomena of liver changes of a necrotic character was especially pronounced. The most important prodromal symptoms were headache above the eyes, disturbance of the special senses, cerebral symptoms, faintness, and general headache; while in 149 of the 161 cases no distinctly premonitory symptoms have been observed. As a rule, however, symptoms of cerebral disturbance were most significant and most reliable as indicating the approach of eclampsia. In 113 cases, albuminuria in varying intensity was observed; in 8 cases eclampsia developed first after the birth of the child; in 3 convulsions came on as late as forty-five to fifty-six days after childbirth. In the cases developing after labor, one patient died; 12 cases of eclampsia are reported without convulsions, with one maternal and 2 foetal deaths. In the fatal case chronic nephritis and albuminuric retinitis were present. Autopsy showed multiple ecchymoses in all the organs, especially abundant in the liver and kidneys. In the child that died, eclamptic symptoms developed before death, and autopsy showed the characteristic lesions. Of the 161 mothers, 32 died. In the 8 cases having eclampsia in the puerperal period, 2 died, and there were 12 cases where eclampsia developed without convulsions. If all the cases in which treatment seemed to cut no figure are deducted, there remain 136 cases with 27 deaths. Among the 136 patients were 31 treated by delivery by operation, in whom the birth canal was already dilated before delivery; 29 of these patients were delivered by forceps; one by extraction of the breech; and 1 by bringing down the feet, with extraction. Among these 31 mothers there were 4 deaths. In the greater proportion of cases the birth canal was not dilated when treatment was instituted. Dilatation was effected by Bossi's dilator in 63; in 31 cases by the forceps; in 18 by version and bringing down the child; in 8 by bringing down the feet; in 5 after perforation; and in 1, by expression of an incomplete abortion. Dührssen's incisions were made eleven times, and in 11 cases vaginal Cesarean section was performed. In all, there were

105 patients in whom the birth canal was not dilated when delivery was effected, and among these were 25 deaths, with a mortality of 23.8 per cent. The question as to whether immediate or delayed delivery should be practised, is studied by tables analyzing the results in the two methods. The conclusion is reached that the prognosis for mother and child becomes distinctly worse the longer the operator delays after the first convulsion. In the 146 cases there were 127 with child at practically a viable period; of these 43 perished.

GYNECOLOGY.

UNDER THE CHARGE OF

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The Functions of the Great Omentum.—As the result of his pathological and experimental studies, RUBIN (*Surg., Gyn., and Obstet.*, 1911, 117) concludes in part that the omentum has no spontaneous motility, nor does it possess a demonstrable chemotaxis. It cannot restore vitality to necrotic organs nor vascular supply to those deprived of their circulation. The usefulness of the omentum in inflammatory lesions of the abdomen upon its power to form adhesions about the diseased focus and upon its power of absorbing and eliminating toxic products or destroying them by virtue of its phagocytic elements. The chief functions of the omentum are those of any other mesentery, viz., the fixation of viscera and vascular supply. When the omentum is found adherent to a tumor, the mass is probably inflammatory and not neoplastic. Too much should not be expected from grafts of the omentum; a detached piece rapidly becomes necrotic.

Myoma of the Uterus, with Special Reference to Degenerative Changes.—According to DEEVER and PFEIFFER (*Amer. Jour. of Obstet.*, 1911, lxiii, 257) the symptomless myoma does not require removal. Aside from the general condition of the patient, the decision as regards the advisability of operation depends upon the mortality of operation, the urgency of the immediate symptoms, and the ultimate fate of the growth as regards its degenerative changes. In the most skilful hands the mortality of operation is from 1 to 3 per cent., a factor not to be forgotten. Repeated hemorrhages, extrusion or strangulation of the growth, impaction in the pelvis and infection demand operative intervention. Of the benign regressive changes affecting myomata, hyaline degeneration is the most frequent (11 per cent.) in the series of cases studied. This change affects practically all fibroids which attain any size, but is of no clinical significance until the process goes on to the stage of liquefaction and cyst formation when the augmentation of

symptoms requires operation. Necrosis, which was observed in 3.6 per cent. of the cases, does not increase the danger of operation unless infection is superimposed. Calcareous degeneration was encountered in 2.4 per cent. of the cases. Malignant degeneration, sarcoma, was found in 4 cases, 1.2 per cent. Deaver and Pfeiffer are of the opinion that the tendency to the malignant degeneration has been exaggerated, otherwise sarcoma of the uterus would be one of the most frequent diseases, whereas it is comparatively rare. Associated carcinoma of the uterus was found in 11 cases, 3.1 per cent.; 6 involved the body and the cervix. While a cervical carcinoma can hardly be credited to the presence of a myoma in the body of the uterus, the unusual frequency of fundal as compared with cervical carcinoma warrants the assumption that a well-defined number of cases of cancer of the fundus are precipitated by the presence of myomata.

The Formation of the Corpus Luteum.—MEYER (*Archiv f. Gyn.*, 1911, xciii, 54) concludes from a careful histological study that with the ripening of the follicle, prior to the formation of the corpus luteum, the theca cells exhibit a considerable increase in plasma and fat; later the granulosa cells likewise share these changes, but to a smaller degree, and, in addition, undergo slight proliferation. After rupture of the follicle, the theca interna shows a greater infiltration of fat than the epithelium, but this is soon reversed. In the formation of the corpus luteum it is possible to distinguish the early hyperemic stage, with a small amount of capillary rhexis and lutinous transformation of the granulosa epithelium which proliferates and secretes into the lumen. Then follows the stage of granular metamorphosis through vascularization of the epithelial margin which continues to proliferate and secrete; lutinous infiltration becomes more extensive. Thirdly, the menstrual stage, in which after cessation of capillary dilatation, and with the transformation of the contained blood into connective tissue, the epithelial margin is completely enclosed with the formation of a gland of internal secretion. Lastly follows the stage of involution. These stages merge into one another without sharp differentiation, but can be easily recognized microscopically. Since the theca cells present wide variations and are dependent upon extraneous conditions, the recognition of the individual stages must depend upon a study of the epithelium. In the first stage the theca probably acts as a nutrient medium; with the completion of the lutein margin the theca cells serve as a supporting tissue. The corpus luteum is an epithelial organ of internal secretion. The histological characteristics of the corpus luteum of pregnancy are due merely to its longer duration and are of no significance. True ovulation during pregnancy was not observed.

Tuberculosis and Pregnancy.—SCHAUTA (*Monats. f. Geburts. u. Gyn.*, 1911, xxxiii, 265) states that pregnancy exerts a deleterious influence in the great majority of tuberculous women. Even under the most favorable circumstances, dietetic and hygienic treatment of pregnant women is of only questionable value in checking the rapid advances of the disease. It is Schauta's opinion that the indication for an early abortion is given in every case in which the diagnosis of tuberculosis is

definitely established. The termination of pregnancy during the later months is not only useless, but may be harmful, with the exception of those rare cases in which it may be necessary to save the child. As regards the best method of emptying the uterus, he recommends the anterior colpohysterotomy. To prevent further conception, the tubes are doubly ligated and divided at the isthmus and their uterine ends covered over by the round ligaments.

Distention Changes in the Duodenum in Chronic Intestinal Stasis.—

In several cases LANE (*Surg., Gyn., and Obstet.*, 1911, xii, 221) has observed distention of the duodenum associated with intestinal stasis, which he at first attributed to the damming back of the contents of the ileum by the obstruction of its termination. Later he was led to conclude that the duodenal distention was due to a compression of its third portion by the strain exerted upon it through the mesentery of the small intestine or by the pull of the jejunum. Duodenal distention is not infrequently associated with ulcer, and the symptoms are similar to those produced by ulcer. Lane presents eleven skiagraphs illustrating a typical case in which posterior gastro-enterostomy was performed.

Radiotherapy in Gynecology.—According to JAUGEAS (*La Gyn.*, January, 1911) the ovaries as well as the thyroid and hypophysis are directly influenced by radiotherapy. This form of treatment is especially adaptable to myomata. Its use depends on the clinically established relation between the ovaries and the development of uterine myomata and on the clinical and experimental results of the action of the x -rays on the ovary. Experiments in animals have shown that exposure of the ovaries to the x -rays is followed by a degeneration of the follicle epithelium, death of the ova, sclerosis of bloodvessels, leading to total disappearance of all follicles. Observations in women have shown that a similar degeneration of follicle epithelium occurs, many follicles being entirely replaced by hyaline tissue. Also small capillary hemorrhages are found in the cortex which might account for some destruction of tissue. But little is definitely known of the action of x -rays on myomata; in tumors with young cells and active karyokinesis the growth may be inhibited as in other neoplasms. Nuclear degeneration, cellular destruction and fine hemorrhages have been observed in myomata after treatment with the x -rays. There are some cases in which radiotherapy has no effect in lessening the hemorrhages, which is an indication for the cessation of treatment. X -rays and surgical treatment should not oppose each other, since each has its indication. In cases of small myomata scattered through the uterine wall, fibrous degeneration of the uterus and of sclerotic uteri in which hemorrhage is the dominant symptom, radiotherapy is indicated; in large myomata of recent growth it may be justifiable if no symptoms of compression, et cetera, demand immediate relief, since the treatment must extend over months. Old, slowly growing tumors are, as a rule, little affected by radiotherapy, and generally require surgical treatment. Results are usually obtained more quickly in women near the menopause than in those younger.

OPHTHALMOLOGY.

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Pigmentation of the Iris, Cornea, and Lens.—VOSSIUS (*Centralbl. f. prak. Augenhk.*, September, 1910, p. 257) finds that following operations upon the iris in iritis, glaucoma, cataract, as well as after injuries of the eye involving tears of the iris, a peculiar, almost jet-black deposit of pigment occurs upon the anterior surface of the iris; the pigment is most saturated in the pupillary region, and is occasionally observed upon the posterior surface of the cornea. The pigment is derived from the retinal pigment layer of the iris, particles of which occasionally become detached, sink down at the bottom of the anterior chamber, or float freely in the aqueous humor, or attach themselves to the anterior surface of the iris. At times such pigmentation is observed upon the iris and posterior surface of the cornea in iritis without iridectomy; very rarely the pigment is also found upon the posterior surface of the lens without iritis. Such pigmentation may remain unchanged for years. A deposit of pigment also occurs occasionally upon the anterior surface of the iris, when bits of iron remain in the eyeball with siderosis of the iris; and also after absorption of hemorrhages into the anterior chamber. In siderosis, the color of the pigment is dark sepia brown; following absorption from hemorrhages, the shade ranges from reddish brown to chestnut brown. This pigmentation is not identical with the coarse light yellowish red and brownish pigment points found near so-called pigment nevi, or without the latter. In siderosis the particles evidently consist of oxide of iron; in hemorrhages into the chamber they are composed of hemosiderin, such as is found by microscopic examination, in the form of small brownish particles with crystal reflex upon the anterior surface and within the anterior layers of the iris.

The Path of Entrance Into the Eye of the Virus of Rabies.—KOENIGSTEIN and HOLOBUT (*Archiv f. Augenhk.*, April, 1910, p. 6) find, with Fukala and Kraus, that next to subdural inoculation, insertion into the eye gives the most certain results. General infection may be avoided if the cornea is abraded or destroyed within six hours after inoculation. The virus enters the anterior chamber and reaches the encephalon by way of the optic nerve. Preliminary section of the optic nerve, as well as section of the same or enucleation a short time after insertion of the virus into the cornea, will prevent generalization. Both subdural and corneal inoculation render an emulsion of the optic nerve infectious.

Ocular Mycosis.—MORAX (*Archiv. d'ophtal.*, October, 1910, p. 654) reports two new cases of primary palpebral sporotrichosis; in both the diagnosis was established by cultures showing *Sporothrix Beurmanni*; in the first case treated by iodide of potassium, the infection disappeared at the end of three months. The same author observed a third case of mycosis of the cornea. The patient, aged forty years, showed a white spot involving a quarter of the cornea, resembling a false membrane, accompanied by slight lypopyon; the galvanocautery effected a cure.

Accommodative Changes in Man.—HESS (*Archiv f. Augenhk.*, lxx, 170) was able to observe the accommodative changes in the lens, ciliary body, and pupil with the binocular loup in an eye removed immediately after death; the globe was divided and strongly illuminated from behind, and the cornea laid upon electrodes. He saw clearly how the ciliary processes moved forward and toward the axis; the contraction of the pupil reached its maximum before the advance of the ciliary, while the latter slightly preceded dilatation. Although the subject was sixty-four years old, and hence deprived of accommodation, the ciliary body was still capable of active contractions.

The same observer also examined eyes by a similar arrangement in some of which eserine and in others atropine had been instilled *ante exitum*. The first pair belonged to a subject aged twenty, the second forty-two, and the third sixty-eight years respectively. In the eyes from the twenty-year-old individual, the equatorial diameter of the one treated with eserine was 0.4 to 0.5 mm. smaller than the atropinized eye and the same was the case with the ciliary circle; in the eyes from the individual, aged sixty-eight years, there was no perceptible difference in these structures. This is the first instance in which the accommodative changes of the human lens were observed under fixation. Hess believes that this method is very promising as regards many other questions.

Relation of the Anterior Region of the Corpora Quadrigemina to the Pupillary Reflex.—LEVINSOHN (*Centralbl. f. prak. Augenhk.*, March, 1910, p. 92) finds from experimental researches that the course of the centripetal pupillary fibers can be followed only as far as the external geniculate body. The continuation of these paths, particularly their connection with the oculomotor nucleus, is not known. It is certain, however, that the entire anterior quadrigeminal body, inclusive of the layers extending to the base of the aqueductus sylvii, is not concerned with the conduction of the light reflex of the pupil.

Glaucoma Cured by Simple Section of the Iris.—ABADIE (*Archives d'Ophtal.*, August, 1910, p. 518) has always maintained that the curative effect of iridectomy in glaucoma is due to section of the circular nervous plexus which the iris is supposed to contain. If this is the fact, more or less extensive excision of the membrane is unnecessary; a simple section should suffice, extending from the pupillary border to the ciliary insertion, thus dividing the circular nervous network which the cut traverses. He reports a case which seems to confirm this hypothesis.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Bacteriology of Pasteurized and Raw Milk.—AYERS and JOHNSON (*U. S. Department of Agriculture, Bureau of Animal Industry, Bull.*, 126) have studied the bacteriology of commercially pasteurized and raw market milk. In undertaking these studies they have deviated somewhat from the usual custom of isolating large numbers of individual strains or species of bacteria and then studying these in great detail. They have, on the contrary, approached the problem from the point of view of what the bacteria actually do in the milk, and they find that there are three principal types of bacterial activity represented—bacteria which form considerable amounts of lactic acid, bacteria which peptonize the milk, and finally, the third group, which produce a slightly alkaline reaction, but bring about no further change in the milk. They have summarized the advantages and objections to pasteurization as follows: The principal advantages are (1) protection from infection with the diseases usually transmitted by milk; (2) reduction of bacteria, and, as a consequence, of the infantile death rate; (3) improvement in the keeping quality of milk. The objections to pasteurization they have summarized as follows: (1) It is believed that the lactic acid bacteria in raw milk, which eventually sour the milk, exert a restraining influence on peptonizing bacteria which would otherwise cause putrefaction of milk. Peptonizing bacteria when freed from the restraining influence of the lactic acid organisms may increase to large numbers and produce toxins and poisonous decomposition products. (2) The pasteurization of dirty milk, while reducing the bacterial numbers, does not destroy the toxins or other products of bacterial growth. (3) Careless methods of handling milk for pasteurization may result in serious contaminations. (4) Pasteurization may be used simply to cover up dirty milk. It may encourage dirty methods in production and retard the extension of sanitary supervision. (5) Milk which has not been sold may be pasteurized or even re-pasteurized and its faults hidden. (6) Bacteria may increase more rapidly in pasteurized milk than in raw milk. (7) Undesirable changes may be produced by heating which result in making the milk less digestible, particularly in the case of infants. Ayers and Johnson conclude their paper as follows: (1) Commercially pasteurized milk always sours, because of the development of lactic-acid bacteria, which, on account of their high thermal death point, survive pasteurization, and perhaps in some cases, because of subsequent infection with acid-forming bacteria, during cooling and bottling. The acid development in an efficiently pasteurized milk is about the same as that in a clean raw milk. But sometimes a strong, old taste develops, which is probably due to the development of alkali or inert bacteria. The old

taste, however, is not characteristic of pasteurized milk, for it may be noticed as well in clean raw milk when held under similar conditions. The less efficient the pasteurization process the more closely does the acid increase of the heated milk approach that of a dirty raw milk. (2) The relative proportion of the groups of peptonizing, lactic acid, and alkali or inert bacteria is approximately the same in efficiently pasteurized milk as it is in clean raw milk. In both cases the alkali or inert forms constitute the largest group, the lactic-acid bacteria next, while the peptonizers are in the minority. When both of these milks—the efficiently pasteurized and the clean raw milk—are held, the group relations change; but if the changes which take place are compared it will be found that they are the same in each. At the time of souring, the group proportions have changed so that the lactic-acid bacteria constitute the largest group, with the alkali or inert forms next in order, and the peptonizers in the smallest proportion as initially. In both of these milks the group of peptonizers may increase slightly in its proportion to the other two groups during the first two days, but it then gradually decreases and always forms the smallest group. When milk is less efficiently pasteurized the position of the groups may be reversed so that the lactic-acid bacteria constitute the largest group, with the alkali or inert forms next in order; but here again the peptonizers form the smallest proportion of the total bacteria. This group arrangement is the same in a dirty raw milk. The more efficient the pasteurization, the smaller the percentage of lactic-acid bacteria; and similarly, the cleaner the raw milk, the smaller the percentage of lactic-acid bacteria. (3) The peptonizing bacteria are present in smaller numbers in the inferior grades of commercially pasteurized milk during the first twenty-four hours after receiving than in raw milk of the same quality, and the peptonizers may increase to slightly higher numbers in the pasteurized milk when held several days than in the raw milk of high initial lactic-acid bacteria content; but it should be remembered in this connection that milk is usually consumed within twenty-four hours after delivery. The number of peptonizers in a good grade of commercial pasteurized milk on the initial count and on succeeding days is approximately the same as in a clean raw milk when held under similar temperature conditions. (4) Lactic-acid bacteria of high thermal death point are found in milk and may be easily isolated by special methods of procedure. From these experiments it was found that when milk is heated for thirty minutes at 60° C. (140° F.) and plated, the percentage of acid-forming organisms that resisted the heating ranged from 0.001 to 18.91, the average being 4.8 per cent. of the total acid colonies. When heated at 65.6° C. (150° F.) the range is from 0.001 to 3.13 per cent., the average being 0.74 per cent. of the total bacteria. It must be remembered that these figures are based upon acid colonies, and these are not necessarily all true lactic-acid bacteria. The thermal death point of one lactic-acid organism which was isolated from milk is 74.4° C. (166° F.) in broth and 75.6° C. (168° F.) in milk when heated in Sternberg bulbs for thirty minutes. When heated for ten minutes in milk the thermal death point is 77.8° C. (172° F.). These heat-resisting lactic-acid bacteria play an important part in pasteurized milk and undoubtedly account to a large extent

for its ultimate souring. (5) All milk, whether pasteurized or raw, must necessarily be infected during cooling and bottling, by bacteria in the receiving tanks, in the pipes, on the cooler, and in the bottles; but the low bacterial counts obtained from pasteurized milk in these investigations show that the reinfection must have been very small. (6) It is manifestly unfair to conclude that bacteria increase faster in pasteurized than in raw milk, simply from a comparison of the ratios of bacterial increase. If a pasteurized milk with a low initial count is compared with a raw milk of high bacterial content, then the ratios of increase may show that the bacteria in the heated milk do increase faster; but if the same pasteurized milk is compared with a clean raw milk with a low count, then the ratios of increase will be found to be approximately the same. From the results of this investigation it is evident that bacterial increase in an efficiently pasteurized and a clean raw milk is about the same when the samples of milk are held under similar temperature conditions. This question of the relative growth of bacteria in raw and pasteurized milk can be properly settled only by a long series of comparisons of samples of milk with approximately the same bacterial count and similar bacterial group percentages. (7) The "holder" process of pasteurization is superior to the "flash" process. With the "holder" process a high efficiency may be obtained with a low temperature, while to obtain the same efficiency with the "flash" process a high temperature would be required. A temperature of 62.8° C. (145° F.) for thirty minutes seems best adapted for efficient pasteurization. (8) Considering the low counts of bottled commercially pasteurized milk and the similarity of the bacterial group proportions to those of clean raw milk, the former cannot be classed from a bacteriological point of view as inferior to commercial raw milk. Pasteurized and raw milk should, however, always be bottled, and should not be allowed to be sold as "loose" milk from stores. (9) Pasteurization should always be under the control of competent men who understand the scientific side of the problem. It is believed that ignorance of fundamental bacteriological facts often accounts for inefficient results rather than a willful lack of care on the part of the dairyman.

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ORIGINAL ARTICLES.

MYOMA OF THE UTERUS, WITH SPECIAL REFERENCE TO
DEGENERATIVE CHANGES.¹

BY JOHN B. DEAVER, M.D., LL.D.,

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WITH AN ANALYSIS OF CASES.

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It has always been my contention that a woman who possesses a fibroid tumor that is symptomless and discovered only by accident displays good surgical judgment if she refuses to submit to its removal. This opinion has received support from most well-considered contributions to the subject. In the admirable work on "Myomata of the Uterus," recently issued by Kelly and Cullen, the autopsy records of the Johns Hopkins Hospital have been reviewed with reference to the general frequency of myomatous tumors. It was found that of 742 women over twenty years of age, dying from general causes, myomatous growths of the uterus were present in 148, or about 20 per cent. From this and similar statistics it is apparent that the incidence of fibroids is much greater than is the incidence of troubles caused by them.

Granted that the mere presence of a demonstrable fibroid is not in itself an indication for operation, we are confronted with

¹ Read at a meeting of the American Association of Obstetricians and Gynecologists, Syracuse, N. Y., September 22, 1910.

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the task of assigning the proper indications. Leaving aside the general condition of the individual patient, which is a constant factor for consideration in all surgical procedures, our decision must be compounded of three factors, viz.: The mortality from the operation itself, the urgency of the immediate symptoms, and the prognosis of the disease if unchecked by active intervention. As for the first consideration, we find that the mortality of operations in this class of cases as they now come to us is in the best hands from 1 to 3 per cent. In the hands of unskilled or occasional operators it is necessarily somewhat higher. This mortality, while not large, is sufficient to make us cautious in the selection of cases. In all but ultra-conservative quarters it is not sufficient to cause delay of operation in such cases as severe sudden hemorrhage, or smaller hemorrhages so frequently repeated as to bring the patient into a condition of grave anemia, nor in the case of extrusion of the tumor or strangulation by twist of a pedunculated growth. Impaction of the growth in the pelvis also may cause such severe symptoms as to defy mere palliative measures, and when sepsis is implanted upon a myomatous condition of the uterus it assuredly requires the aid of operation. Other and rarer complications may make operation the wiser course, but all these are conditions which are announced to both patient and physician in unmistakable terms, and our best physicians who combine boldness and prudence will not be long in arriving at a conclusion as to the need for operation, nor will they shirk their duty in advising it.

The day is past when surgical treatment must justify its plea for preference in these cases, even though there is still a disinclination among some to follow the plain indications. The cause of this disinclination is not in the case, but in the man himself. I venture to predict that there will never be devised for any ill or disorder so perfect a treatment that it will receive the unanimous assent and support of the body of physicians. Indecision and minds that work on the bias will always be with us, as in every other calling or vocation. I will not, therefore, take up time in trying to convert those who deny the means of salvation, and will rather devote myself to an examination of the third factor in decision, namely, the prognosis of fibroid disease of the uterus in so far as it relates to the behavior of the tumors themselves, or to pathological conditions caused by their presence. This is a most important question. To anticipate dangers before they arrive and to devise means of warding them off is to approach the ideal in medicine and surgery as well. However skilful a physician may be in the presence of actual danger he is not exercising his highest function unless he is so armed with a knowledge of the probable developments of disease as to enable him often to steer his patients away from the rocks. This is the art of prognostics which Hippocrates never ceased to praise, calling it even God-

like, probably because it represented the nearest approach to the divine knowledge of the future which could be possessed by man. This is at the bottom of the great movements in preventive medicine, and to a certain extent has been adopted in surgery. Thus, the removal of a chronically diseased appendix is a high development of prognostics, and comes from our knowledge, painfully acquired, of the relative risks of such a condition as compared to operation.

An effort has been made to place myomatous disease of the uterus among the conditions which demand a preventive operation because of the probability of malignant degeneration of these tumors themselves or of associated tissues.

For consideration we may divide these pathological changes into: (1) Degenerations of the fibroids themselves, which may be either (*a*) non-malignant or (*b*) malignant; (2) malignant disease of the body or the cervix of the uterus associated with a fibroid condition of that organ.

My last 345 consecutive operations for myoma of the uterus have been analyzed chiefly with reference to this point; 250 cases immediately preceding those upon which this paper is based were made the subject chiefly of a clinical analysis. As the pathological data of this series were found to be less complete than in the present series, they have been disregarded since we felt that the smaller number of cases would give the truer picture from a pathological standpoint.

Hyaline degeneration is the most frequent of the benign regressive changes affecting fibroids. It has been noted as present in a marked degree in 37 cases, or about 11 per cent. This does not represent the true incidence of the condition, since early hyaline change was not specially noted. Practically all fibroids which attain any size will show this condition in some part of the growth. It is chiefly of pathological interest, and possesses no clinical significance until it goes on to the stage of liquefaction and cyst formation. When this occurs the tumors often take on rapid increase in size, and symptoms are usually augmented in proportion. The product of this melting process is a material which varies from a gelatinous consistency to a thin, watery fluid. Tumors filled with the gelatinous material are often said to have undergone myxomatous degeneration, while those in which the thinning process has gone on to the production of watery fluid are termed cystic. In some series both conditions are together recorded as cyst formation. In our series we found nine instances of myxomatous change and 3 pronouncedly cystic, 12 in all (3.6 per cent.). This corresponds rather closely with Noble's figures in his extensive collection of 2274 cases of fibroids, in which he found approximately 2.6 per cent. of cystic changes. This condition, when it arises, demands operative treatment. Cullen reports a case in which the tumor weighed eighty-nine pounds and was mistaken for an ovarian

cyst. It is chiefly those cases when one is dealing with a single soft symmetrical tumor of moderate size that are so difficult to distinguish from pregnancy. The simulation may be perfect and the distinction impossible even with the abdomen open.

These changes are probably due to slowly failing nutrition of the growth. When the nutriment is more suddenly cut off, the tumor undergoes necrosis. If this occurs in such a way that extravasation of blood takes place into the tissues, the tumor presents a peculiar brick-red color, which has caused it to be called red necrosis. If blood is not present in excess the tissue elements simply lose their definition and show the ordinary picture of coagulation necrosis.

Usually necrosis affects only a limited portion of the tumor and gives rise to no symptoms. In some cases, however, the growth may perish en masse, and this is generally accompanied by more or less severe symptoms. This extensive necrosis is most apt to affect pedunculated myomas where the mechanism is usually apparent, being due to strangulation of the blood supply or infection. Occasionally, however, an intramural fibroid will undergo sudden necrosis, without obvious reason. This is more apt to occur during pregnancy. Necrosis of this sort is a serious condition, chiefly because of the danger of secondary infection. A necrotic fibroid which projects into the cavity of the uterus or possibly from the cervical canal always becomes infected, and it is important not to mistake the foul sloughing mass for an inoperable carcinoma. Christopher Martin found necrosis occurring in fibroids in about 4 per cent. of cases considered. Noble found it in 119 cases (5 per cent.). In our series it occurred twelve times, or 3.6 per cent. It does not materially increase the danger of an operation unless it be already accompanied by infection.

In sudden necrosis of an entire tumor, one finds usually definite symptoms pointing toward interference, such as pain, vomiting, rapid increase in size of the tumor, tenderness, and often some fever. When necrosis takes place in successive small areas it is followed by a deposition of calcium salts, which gives rise to the so-called calcareous degeneration. This we found eight times (2.4 per cent.). It is practically a spontaneous termination of the life of the tumor, and is rather to be welcomed than otherwise.

If we add together all noteworthy benign degenerations occurring in this series we have a total of 30, or 9.6 per cent. This is not to be interpreted to mean that approximately 10 per cent. of all fibroids will show such degenerative changes, but that of a series of cases which are considered under present standards to require operation, about 10 per cent. are causing trouble largely as a result of degenerative changes which have occurred in them.

Malignant degeneration of fibroids is a matter of much greater importance if it be proved to be of frequent occurrence. The

only malignant change which a fibroid itself can undergo is, of course, transformation into a sarcoma. Martin in his recent paper concludes that this occurs in approximately 4 per cent. of all cases. He quotes statistics as follows: Winter found sarcomatous change in 4 per cent. of 500 myomas; Martin found 6 in 205 cases; Cullingworth, 1 in 100; Scharlieb, 6 in 100; Haultain, 2 in 120; Hirst, 3 in 189; McDowell, 20 in 1000 cases. He, himself, encountered 9 cases in 380 abdominal sections for myoma. These collectively total about 2 per cent. of sarcoma presumably arising upon a myomatous base. He goes on to say that "probably many other cases thought to be primary sarcomata have originated in unrecognized myomata," and from this assumption justified himself in raising the true proportion to 4 per cent. Bland-Sutton, however, has taken a directly opposite view, and states that quite possibly sarcomas which have been considered as derived from preceding myomas have been sarcomatous from the beginning. Noble, in his large tabulation, found only 34 cases of sarcoma, or about 1.5 per cent. It is not stated that these cases were all instances of sarcomatous degeneration of myomas, and it is quite likely that some at least were mere associations. Kelly and Cullen found sarcomatous degenerations or association in 17 out of 1400 cases (1.2 per cent.). In our series we found 4 cases, 1.2 per cent., which were diagnosticated pathologically as sarcoma.

In the first case the tumor, which was a small round-celled sarcoma, gave no evidence of its being derived from a myoma. The second case was a myxosarcoma which also showed no evident connection with an antecedent, myomatous condition. It seemed rather probable that such was not the case. The third case involved the ovary, and it is difficult to see what possible connection the fibroid condition of the uterus could have had in the origin of such a different condition. In the fourth case the sarcoma was in no way connected with the uterus. Clinically there was nothing to suggest such a malignant change, and the patient has remained without recurrence. In this case the patient was operated on primarily for a huge ovarian cyst, and the uterus found after section to be the seat of numerous fibroid nodules. The condition had been present for years, and the tissues were very atypical in appearance. Under such conditions only those who are skilled in microscopic work know how difficult it may be to set the exact boundary between a malignant and a non-malignant change. The personal equation of the pathologist must be taken into account in such cases. It is only thus that I can account for the high percentage of sarcomatous changes found by some authors who counsel minute microscopic examination of various parts of all the tumors present. I am aware that it is by no means impossible for such a transformation to take place, but I cannot believe that this tendency is so marked as is stated by some authors. If it were true, then

sarcoma of the uterus ought to be one of the most frequent of diseases, whereas it is comparatively rare. Simply to make use of the figures already given, taking 20 per cent. as the absolute incidence of myoma of the uterus in women over twenty, if 4 per cent. be the tendency of myoma toward sarcomatous change we should find sarcoma in 4 per cent. of 20 per cent. of all women, or 8 per cent., which is a *reductio ad absurdum*. I do not desire to cast discredit upon the findings of anyone, but I must point out that either the experience of those who find such marked proportions of sarcoma must be exceptional or else that there is a subtle source of error in the standards of diagnosis. I may state that for years every fibroid uterus which I have removed has been subjected to careful gross and microscopic examination in our laboratory at the German Hospital.

Another point which is urged for the preventive removal of fibroids is the increased tendency to uterine cancer found in myomatous uteri. That this is a real danger cannot be denied. The present series of cases shows 11 instances of carcinoma associated with myoma (3.1 per cent.). Of these, 6 (1.7 per cent.) involved the body, and 5 (1.4 per cent.) were situated in the cervix. These figures agree very closely with Kelly and Cullen, who found in 1400 cases of myoma 43 of associated carcinoma (3 per cent.), of which, 25 (1.7 per cent.) were in the body and 18 (1.3 per cent.) in the cervix. Martin found 6 cases of carcinoma in 380 (1.6 per cent.), while Noble, in his large collection, found 2.8 per cent. of carcinoma, and among his personal cases 4 per cent.

This is an alarming incidence of a desperate condition with one which is relatively innocent, and if we are able to incriminate myoma in the causation of cancer it will be a heavy stigma. The instances of cervical carcinoma can hardly be credited to the presence of myomata in the body of the uterus. Not only is it difficult to imagine any way in which a fibroid should exercise such a malign influence upon the cervical epithelium, but clinically we gain no impression that such is the case. Bearing in mind that the uterus is the most common site of carcinoma, as established by the large statistics of Welch, who found that cancer of the uterus furnished 29.5 per cent. of 31,482 cases of primary cancer, we must be prepared to find it associated with such a frequent pathological condition as myoma, which furnished at least a tenth of all gynecological work.

This association should cause no more remark than the simultaneous presence of carcinoma of the breast, stomach, bladder, or rectum, all of which have been noted in a number of instances.

Concerning carcinoma of the fundus, the case is different. If the presence of myoma does not influence the development of malignancy in the uterine epithelium, we should expect that the ratio of cervical to corporeal cancer would remain unaltered. This

ratio is estimated at from 4 to 1 (Cullen) to 10 to 1 (Martin). My own statistics are more nearly in accord with the lower ratio, but in any case there can be no doubt that cervical cancer predominates largely over that which is primary in the body of the uterus.

Now, of the cancers which are found complicating a fibroid condition of the uterus, we may see by a glance at the above figures that the preponderance is reversed and fundal cancer is found to be more frequent than that of the cervix. It seems a fair assumption, and one which is also suggested by the known tendency of chronic nutritional and irritative influences to excite malignant change, that a well-defined number of cases of cancer of the body are precipitated by the presence of myomata. This, to my mind, is the most serious of the degenerative processes set in motion by a fibroid tumor, since it always arises insidiously, as do all cancers of the fundus. Sarcoma is no less insidious, though less common as a derivative of myoma. Together they constitute a menace to life of no mean degree, and though the results of observation and analysis of this series of tumors do not support the pessimistic views of some gynecologists, the danger of malignant changes due to myomata is a fact which cannot be disregarded. The early operation for fibroids does not rest upon this factor alone, and high statistics of degeneration are not needed to support it. "A good cause can sustain itself upon a temperate dispute." The only point in which I would differ from those who believe in the higher percentage of malignant change is in not advocating the removal of an accidentally discovered fibroid that is giving no symptoms. This is not a large class of cases, and therefore not a very important difference. Any tumor that begins to give trouble or atypical symptoms, even if only an irregular discharge, I believe should be removed. The tendency toward malignant degeneration gives me one of the elements of my belief. The remainder are furnished by the greater frequency of troublesome non-malignant degeneration, the likelihood of hemorrhage and chronic anemia with cardiac and vascular disturbances, the frequency of pain and more or less dangerous pressure effects upon the urinary tract, the intestines, and surrounding organs, the proved failure of fibroids to cease from troubling with the menopause, and the certainty that in a large percentage of cases delay merely means operation later under less favorable conditions.

THE CEREBRAL FORMS OF POLIOMYELITIS AND THEIR DIAGNOSIS FROM FORMS OF MENINGITIS.

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DURING the first epidemic of poliomyelitis and in the recurrent outbreaks in New York and vicinity, there have occurred here and there a number of cases, which have been of great interest because of their close simulation to certain cerebral conditions, which we shall mention later. I refer to those cases of poliomyelitis which belong more particularly to the cerebral group of this affection. Polioencephalitis or encephalitis, as it is called, was first brought into closer relationship with poliomyelitis by Medin. In the large Swedish epidemic of 1905 there were many of these cases, and Medin, in his early writings insisted upon the general identity of this set of cases with poliomyelitis as it was then known. His assumptions were at first disputed by men of no less genius than Henoch, who thought that Medin in describing the cerebral forms of poliomyelitis as identical with the spinal forms in etiology and pathology had rather committed an error of clinical observation and mistaken his cases for something of another character. How certain and true the original observations of Medin have been, time has shown, and Harbitz and Scheele have proved beyond question that the infectious agent producing epidemic poliomyelitis may extend to any part of the cerebrospinal system, and may affect both the gray and white matter of the brain and cord. Moreover, there is in all cases of poliomyelitis a real meningitis; that is, the processes of infection expend themselves on the membranes of the brain and cord. There is inflammation and infiltration of these structures, and from the vessels of the pia, the toxic or infectious agent enters the tissues of the brain and cord, there effecting changes of greater or or lesser severity. Thus, the consequent symptoms will differ in sets of cases according to the localization of the inflammatory processes at play.

The cases to which I especially desire to call attention are those in which the structures of the brain and medulla and pons are affected, leaving the cord for the most part, unaffected permanently. These cases have been previously described by various writers as encephalitis or polioencephalitis superior or inferior of Wernicke or poliomyeloencephalitis of Strümpel. We may group all these descriptive clinical pictures under the entity of polioencephalitis. This would also include the Pontine forms of encephalitis of Oppenheim. The general picture of polioencephalitis is cerebral, the symptoms are cerebral symptoms with, in certain cases, added palsies. Thus, if the nuclei of the ocular motor nerves

are affected, we have with the cerebral symptoms, an ophthalmoplegia of greater or lesser extent, identical with what Wernicke described as poliocephalitis superior. If the nuclei of the facial nerves are affected and the gray matter in the floor of the fourth ventricle, the cerebral symptoms are supplemented by facial palsies, and thus there is produced the picture described by Wernicke as polioencephalitis inferior. If the process extend still further down, it may involve the nuclear masses of the hypoglossus and more vital nuclei, and then symptoms of paralysis identical with acute bulbar paralysis are produced. Certain it is that the forms of polioencephalitis will merge into one another. Thus, cases occur in which there are isolated palsies such as those of the muscles, one or other of the eyes, and then cases occur in which eye and facial nuclei muscles are involved and others in which all these and bulbar symptoms occur. The last group rather number the fatal cases, though I have seen a number of bulbar cases recover.

To return to the theme: The cases which are limited in their extent of involvement of the ocular and facial nuclei, and which are accompanied by cerebral symptoms are those which to me have been of greatest interest, because in such cases of polioencephalitis, I have had the greatest difficulty in face of the cerebral symptoms accompanied, as they were after a while, with nuclear palsies to differentiate them from forms of meningitis either of the acute suppurative (meningococcic) variety, or the tuberculous forms of the disease. In fact, in some cases the clinical similarity of forms of polioencephalitis with forms of meningitis is so close that it is only by careful observation that we can differentiate the two, and then only with a possibility of some doubt. In order to facilitate clinical study of polioencephalitis, it will be best to first draught in outline the general history of these cases.

A child in previous good health without any marked prodromal symptoms develops fever which may be quite high or may be moderate in degree. There may be complaint of some headache, there may be vomiting. Such a child will continue for twenty-four hours to be up and about, and after this initial period it is noted that the fever continues as does also the headache, and after a time the patient is too sick to be about, complains of tired feeling and goes to bed. It is then noted that the sopor deepens, and then the temperature may subside to the normal or continue a little above the normal. In some cases from this time on, the history reads that the patient is at times delirious, irrational, complains of headache, and resents being disturbed. There is extreme hyperesthesia. Some patients complain of pain in the nape of the neck, there is marked rigidity and Kernig sign in the lower extremities with signs of a mild hydrocephalus (MacEwen). Such patients may have a maudlin delirium, lie crouched in bed and refuse to take food. Close examination may discover isolated ocular palsy in some cases,

and this is the only objective palsy present. In other cases with palsy of some of the ocular muscles there is slight facial palsy of one or the other side, and in still other cases these palsies may be combined with a very mild weakness of one or the other upper extremity. After a week or two the patient gradually becomes more rational, the sensorium is brighter and they begin to recognize objects and talk rationally. If, during the illness, the patient is caused to stand, there is noticed a very marked ataxia and vertigo with Romberg's symptom. As convalescence is established the ataxia is the last symptom to improve. The hydrocephalus may persist, the compromised mental capacities may not return to the absolute normal as soon as one would expect. The temperature has, during the illness directly following the period of invasion, been normal, or in exceptional cases there may have been a rise of 2 or 3 degrees with a fall to the normal daily for a week or more. As the patients convalesce they are able to sit up, this not having been hitherto possible. Speech is more distinct, due to the retrograde of the ataxia.

This is a rough sketch of the common picture. When recovery is established there may remain only a strabismus, or a very mild form of ataxia in the gait, an uncertainty as it were. In one or two of my cases there was a slight atrophy of the deltoid group of muscles. In some cases I have seen optic neuritis such as choked disc in the course of the disease, and this also may retrograde; the eyesight may be entirely restored. In other cases the eyesight which has failed during the illness may progress to absolute blindness, and this in turn, may slightly improve, as in one of my cases, so that after a lapse of months the eyesight may have improved from absolute blindness to the ability to distinguish gross large objects. In another group I have seen a complete ophthalmoplegia with dilatation of the pupil of the affected eye.

I have related enough of the symptomatology of this form of encephalitis or polioencephalitis to show how close the similarity to a cerebrospinal meningitis may be, the sudden onset, the high fever, the rigidity of the neck, the headache, the Kernig all run close to the symptom complex of a meningitis, and yet close study will show some differences. There is in polioencephalitis, a short preliminary period in which the patient having had a high fever, continues to be about. There is also an increasing sopor which extends over days; this is quite unlike the onset of a cerebrospinal meningitis. In these two points we can sometimes differentiate between the two diseases. Here, however, the dissimilarity ceases. In a recent outbreak of polioencephalitis in Staten Island these two points stood out quite sharply on the clinical canvas, namely, the period of a day or so of high fever in which the patients did not quite take to bed, and then the period of fever and increasing sopor with the addition of all the symptoms of true meningitis.

Another set of cases of polioencephalitis is still more perplexing inasmuch as they closely simulate another type of meningitis, the tuberculous form. A patient having been in previous good health will develop fever, some vomiting; the fever may be low, 102° or 103° , or high, 104° to 105° . The fever continues for a day or more and then sopor sets in, the temperature drops to the normal, the patient becomes completely unconscious. With this unconsciousness there is marked hydrocephalus, facial palsy, ocular palsy such as strabismus, loss of reflex at the knee, no Kernig, and there is a Babinski reflex. There may be a tache. After five to seven days of illness the picture is the exact counterpart of a tuberculous case. The patient lies absolutely flaccid; there may be but very mild rigidity of the neck, there is Cheyne-Stokes respiration, and absence of reaction of mechanical stimuli in the presence of a normal or slightly raised temperature. After a few days the patient may either succumb, but in many cases may come out of the coma, regain consciousness and power in the extremities. Such a case I have seen.

In another form the patient may have had a very short period of fever, which may have come on suddenly. Then after a few days the temperature falls to the normal, but the patient is noted to be stupid, and to act as if in a trance, there is mild hydrocephalus, but the sopor is the principal symptom. A bright child is noticed to act stupidly, begs to be left alone. There is hyperesthesia. All of this, in the face of a normal temperature. Gradually the patient, after two or three weeks becomes brighter, takes an interest in surroundings, and the ataxia, which in some cases amounts to absolute inability to walk, in others to staggering gait with vertigo, gradually improves. The similarity of these cases to tuberculous meningitis is exceedingly close. There is one very salient point of difference. In cases of polioencephalitis, the onset is sudden. It is especially noticeable that the children have previously been in excellent health when they are attacked within twenty-four or forty-eight hours at the most by the disease. In this respect, the two maladies are far apart. In tuberculous meningitis the onset is gradual, and cases of sudden onset are extremely rare; in fact, I have not seen an authentic case in several hundreds of cases. In tuberculous meningitis, a state of sopor, in which there is some good preservation of intelligence of surroundings, does not last long, but will deepen into coma, whereas in polioencephalitis there is a diminution of the sopor, and finally, after a week or two, the patient is observed to be brighter.

CASE I.—L. D., male, aged five years. Has had rachitis, scarlet fever, and diphtheria. Three years ago had scarlet fever and diphtheria. Tonsils have been removed.

Family History. Negative. Five weeks before admission to hospital, was taken with high fever, headache, and prostration. The

fever apathy continued for two weeks, during which time the child vomited frequently. The fever then ran a lower course and the child became somewhat brighter. But the child complained of severe headache, vomited occasionally, and was constipated. The patient complained of pain in the right eye and right hand. There have been no convulsions. The child is quiet but parents think it does not sleep. There is sighing respiration.

Status Praesens. The patient is soporose, although he answers questions. There is slight rigidity of the neck, and a tendency to yawn. There is some hydrocephalus on the right side. The reflexes are exaggerated. The pulse is equal, regular, no paralyses noted of any kind. There is slight neck rigidity, tache cerebrale, signs of hydrocephalus on both sides, later on abdomen retracted, a constant tendency to yawn, *left internal strabismus*, patient stuporous but conscious when aroused, no evident paralyses. A lumbar puncture yielded 30 c.c. of clear fluid under some pressure. A day subsequent to admission, the patient was brighter. An examination of the fundus oculi revealed some small retinal hemorrhages suggesting compression of the cerebral retinal arteries, but no choked disk.

Five days after admission, patient was conscious with the above ocular palsy, but interested in surroundings. Some exaggerated knee-jerk. On walking, patient shows some tremors. Complaints of headache, is apathetic, pupils uneven, right larger than the left.

Four days subsequent, still apathetic and complains of headache.

A second lumbar puncture, four days after, the above entry yielded 40 c.c. of clear fluid under same pressure.

Two weeks after admission the patient was still apathetic soporose with neck rigidity and showed slight flatness of the right side of the face.

Eyes examined by Dr. May, at this time, showed optic nerve atrophy, so-called postneurotic atrophy with hemorrhage in the retina. The patient was brighter but there was still some neck rigidity and signs of hydrocephalus.

After four weeks the patient was able to be out of bed; there was some mental obtuseness; marked signs of hydrocephalus; no blindness. There was a distinct ataxia or cerebellar gait; mentality continues below the normal. The patient was up and about without temperature, played with other children.

Puncture fluid examined shows no bacteria; 100 per cent. lymphocytes, some reaction for sugar and albumin.

Van Pirquet tuberculin reaction negative. Blood showed 12,000 leukocytes with a differential count of 51 per cent. of polynuclears on admission. On discharge or near that, the count was 8000 leukocytes.

The temperature was normal after the first twenty-four hours' stay in hospital with the exception of a rise in temperature due to an injection of serum of Flexner given as a safeguard should examination of the cerebrospinal fluid show meningococci.

DISCUSSION. This is a typical case of polioencephalitis resembling very much a tuberculous form of meningitis. There were slight rigidity, stupor, hydrocephalus, and low leukocyte count. The history, however, showed an acute onset five weeks before admission to the hospital. The puncture fluid also showed fully 100 per cent. of lymphocytes, a fact which might very well be linked with tuberculosis. The child was discharged from the hospital, however, well with the remains of the encephalitis in the form of hydrocephalus and impaired mentality. The only paralysis during the illness was ocular.

CASE II.—J. C., aged seven and one-half years, male, admitted December 22, 1908.

Family History. Negative; no tuberculosis.

Past History. None of the exanthemata; was perfectly healthy before the present illness; no pulmonary symptoms; bowels always normal; no urinary symptoms.

Present History for the Past Two Weeks. The parents have noticed that the child has not acted as he did previously, he would cry out suddenly and then laugh. Was pale, no fever; no other symptoms until three days ago when he suddenly became stuporous, cried out, complained of headache. Since then, stupor has deepened, almost constantly moaning and crying; no convulsions.

He has had slight fever; no retraction of head; no photophobia; neck was somewhat stiff; no vomiting; bowels have been obstinately constipated; does not take any nourishment; no twitching of the face and the child does not move its right arm as well as its left; occasionally cries out at night; grinds his teeth.

Physical Examination. Fairly well nourished, lies in a stuporous condition, head somewhat retracted, patient constantly sighs and moans and grinds his teeth, restlessness during examination, seems unable to move the left arm and leg, respiration very irregular, practically no rigidity of the neck, some MacEwen signs, especially on right side, tache present, no Kernig, no hyperesthesia, slight photophobia. Mucous membranes normal, no ataxia, no herpes, ears negative, eyes, both upper lids somewhat ptosed, pupils equal, regular, react to light, eyes have a slight nystagmus-like motion, no strabismus, conjunctivæ somewhat injected, no petechiæ; some excoriation about the alæ nasi; teeth and gums in fairly good condition; sordes on lips; tongue coated. Posterior cervical and a few small axillary glands enlarged. Examination otherwise negative, chest fairly well formed, lungs negative, heart normal, action somewhat irregular and rapid, no murmurs, abdomen retracted, lax, no pain; liver normal, spleen negative.

Extremities: Right arm somewhat spastic, hand held clinched, and as noted above, the child is inclined to move left extremity more than the right extremity; knee jerks exaggerated. No Babinski, no ankle clonus.

December 23. Lumbar puncture, 33 c.c. of clear fluid under moderate pressure removed; tuberculin cutaneous reaction negative. White blood cells, 10,000; 64 per cent. polynuclears.

December 24. General condition somewhat better, less irritable, lies in semistuporous condition, eyes slightly rotated to the left, no rigidity of neck, no Kernig. Second tuberculin reaction negative.

December 25. Examination of the eyes negative.

December 27. General condition fair; still irritable; does not speak; rigidity of the neck; no MacEwen; pupils equal; knee-jerks exaggerated; pseudo-ankle-clonus on the right side; left tendon reflexes increased; physical condition the same.

December 28. Lumbar puncture; 20 c.c. of clear fluid removed.

January 1. The patient for the last few days has periods of stupor and maudlin delirium, in which he cries in a low tone; does not answer questions; does not seem conscious of his surroundings. No paralysis of extremities, with the exception of the right upper extremity, which seems to be weaker than its fellow; patient turns his head from side to side constantly; does not take nourishment; no signs of nuclear involvement in the shape of paresis or paralysis.

January 2. Tuberculin reaction negative, general condition much improved; very noisy and delirious most of the day; had a hot bath and then became brighter; seemed to see and hear when spoken to, but does not speak, he motions with his hands. Very noisy last night; takes nourishment better. Lungs and eyes negative; no paralysis; moves the left arm more than the right; knee-jerks exaggerated.

January 6. Patient, this morning, is conscious, sits up in bed; has a meaningless smile; when he talks, speech is indistinct; has a nasal timbre. Patient does anything he is told to do; has marked loss of power in upper and lower extremities; has a Romberg, when he stands or walks he staggers; his arm, fingers taking on position of athetosis; has no paralysis or paresis of facial muscles; expression of eyes rather vacant, but is conscious and brighter.

January 9. Patient much quieter and brighter; has at times an idiotic smile; speech somewhat indistinct, and has a nasal tone; slight flatness of right side of face; tongue deviates slightly to the right; pupils central—react to light; right grip not as strong as left; no apparent atrophy; uses arm fairly well; the right leg is quite as strong as the left; knee-jerks active, otherwise negative.

January 16. Discharged well, no paralysis, bright, speech still somewhat nasal.

During the whole illness the temperature the first week, from December 21 to 28 ranged from $98\frac{1}{2}$ to $99\frac{1}{4}$ in rectum. After that, remained normal for four weeks, when he was discharged.

The urine was examined three times during the stay in hospital, negative. The lumbar puncture fluid examined twice.

January 2. The first fluid report: Cytology, 100 per cent.; lymphocytes; bacteriology negative; found traces of albumin. The second specimen, 50 c.c. report of sugar reduction, 95 per cent. lymphocytes, mononuclears; no bacteria. Pathologist thinks it has more the character of a transudate than an exudate.

DISCUSSION. In this case there is an imperfect previous history in that no sudden onset with fever was obtained, but there was a period of two weeks of mental irregularities, slight fever, and increasing sopor. The patient on admission to the hospital was unconscious and delirious. This delirium was of a distinctly maudlin variety and cleared up completely, leaving a bright intellect. There was, on admission also rigidity of the neck, vomiting and headache. There was no real paralysis nor strabismus. The reflexes were increased. There were signs of internal hydrocephalus. In this case there was a distinct marked leukocytosis; 30,000 with a polynuclear count of 88 per cent. The puncture fluid also showed a lymphocytosis of 100 per cent. and 95 per cent., sterile to culture; some albumin and sugar. There was, during the course of the affection, slight flatness of one side of the face, some slight deviation of the tongue, and a nasal timbre to the voice, the latter persisted until his discharge.

CASE III.—J. H., aged four and one-half years, admitted to the service, March 2, 1909.

Family History. No tuberculosis; the stepmother has a cough and hematemesis and sees the child frequently.

Previous History. No measles, scarlet fever, pertussis or diphtheria; at the age of six months had pneumonia for five days. *The present illness* began five weeks ago, with occasional vomiting which increased in frequency until the child vomited after each meal. No vomiting in the past two weeks. At that time, the child complained of headache and pain in the abdomen, and has complained of headache up to the present time; had marked cough for a short time two weeks ago. Two weeks ago began to be drowsy and slept a good deal of the day. Was conscious and recognized mother, and asked for food, and played with her toys until five days ago, when she developed rigidity of the neck. For the past five days, child seemed to be brighter and remained in bed, up to that time was up and about; *she does not seem to see well*, no fever or paralyses; the bowels constipated; history of low temperature; no high febrile movement.

Physical Examination by House Physician. General condition poor, though fairly well nourished; marked rigidity of neck with MacEwen, no Kernig; tache cerebrale present; patient lies in a stuporous condition; cannot be roused; makes motions with the hands; does not talk; no hyperacusis; no photophobia; somewhat irritable when disturbed; no eruption on the skin; the ears are negative.

Eyes. Left pupil larger than the right; they react to light; conjunctivæ negative; left internal strabismus. No facial paralysis; teeth and gums in fair condition; tongue coated, moist; throat slightly red; larynx, trachea, and thyroid negative. A few axillary glands to be felt, chest fairly well formed, otherwise negative; heart negative; abdomen negative, liver also; spleen not felt; genitals negative, with slight discharge; no edema of the extremities; knee-jerks exaggerated; there is ankle clonus on both sides; there is Babinski on left side; no paralyses.

Synopsis. Stupor, irritability, rigidity, MacEwen, tache, ankle-clonus, Babinski, exaggerated kneejerks, left internal strabismus.

March 3. Lumbar puncture, 30 c.c. of clear fluid containing floculi was removed. Blood examination: Leukocytes, 30,000; polynuclears, 88 per cent. Fundus of the eyes examined, negative.

March 5. General condition about the same, patient is in bed, stuporous, but can be roused and then is irritable, moderate retraction of head; marked rigidity of neck; MacEwen; slight Kernig, tache present; slight weakness of the left external rectus; no paralyses or paresis; does not void urine; must be catheterized. Respiration cerebral; no clonus; no Babinski.

March 7. Patient is irritable when disturbed, quiet when left alone; has a Kernig; rigidity of neck; Babinski; no MacEwen; cries out. Lumbar puncture, 33 c.c. of clear fluid obtained; contained flocculi.

March 10. Patient is conscious, irritable, and disposed to cry. Sits up in bed when not watched, notices everything around the bed. Slight Kernig with Babinski, especially on right side; rigidity of the neck; takes nourishment; fundus of the eye normal.

March 12. This A.M., is noisy; has distinct retraction of head; rigidity; Kernig; Babinski; opisthotonos; no paralysis of the facial muscles; takes nourishment fairly well; is conscious; pulse slow and regular. White blood cells, 12,200; polynuclears, 71 per cent.

March 14. Patient is more conscious, sits up in bed; no paralysis; there is slight rigidity of neck; slight Kernig; no MacEwen; chest and abdomen negative; takes nourishment quite well. Tuberculin reaction negative.

March 15. Improvement continues; patient sits up and notices objects; is less irritable; today, has slight internal strabismus on the left side.

Patient's general condition is good; patient is more conscious, more or less aware of surroundings; no rigidity; no Kernig; slight MacEwen on left side, no paralyses of limbs. Weakness of the left internal rectus.

March 17. Patient examined today with reference to paralysis; none of the face and extremities found. Strabismus still noted.

March 28. Patient has been up and about the last week; has only a left internal strabismus left. Discharged.

During her stay in the hospital the temperature ranged from 98° to 100 $\frac{4}{5}$ ° in rectum during the first week, and then fell to normal. Pulse and respiration ranged from: respiration, 20 to 30; pulse, 90 to 136; the latter during the fever. When she was up and about the patient's pulse and respiration were 80 and 24 respectively.

The night nurse notes that during patient's illness, the first week, patient slept fairly well, but cried out at night, restless at times, it was necessary to catheterize patient, but after March 6, patient though restless, slept fairly well without any delirium. The urine examined during stay in hospital was negative.

The cerebrospinal fluid examined was negative on first puncture to bacteria; there was a slight amount of albumin present and some sugar.

The second lumbar puncture, March 10, gave a cytology of mononuclears 98 per cent., with no bacteria to culture or to spread; there was some albumin, 2 milligrams and no sugar.

DISCUSSION. I saw this case in consultation: The onset was more or less acute. The subsequent history resembled a tuberculous meningitis, and the diagnosis was placed as a probable instance of this disease. In the hospital the symptoms cleared up, so that the patient who was exceedingly bright was up and about after two weeks. It is to be noted after discharge that, though the patient's eyesight was good she returned in a month with a history of blindness of sudden onset. This after a while, cleared up so that the patient could discern objects clearly. The fundus showed an optic atrophy. In the course of the affection there was a blood leukocytosis of 30,000 with a polynuclear count of 88 per cent. The fluids obtained by lumbar puncture gave a lymphocytotic cytology of 98 per cent., some albumin, no sugar. The urine was negative, as also the lungs. Repeated von Pirquet skin tuberculin test was negative, and the temperature for the stay in the hospital did not exceed the normal after the first week. This case so closely resembled a tuberculous meningitis that a differential diagnosis without prolonged observation seemed impossible.

CASE IV. S. F., schoolgirl, aged eleven years, admitted February 8, 1909 to the hospital.

Family History. Seven other children living and well. No history of tuberculosis.

Previous History. Measles, no scarlet fever, no pertussis, no diphtheria, occasionally sore throat; no rheumatism; no pneumonia; no other complaint.

Ten days ago was taken ill and was in bed with high fever, vomiting, headache, and malaise, then patient was up and about, complaining of occasionally headache until yesterday.

Present Illness. The day before admission she had severe headache, and began to vomit, this continued until this morning, when she had general convulsions, she had a severe convulsion and

had passed into a state of unconsciousness with some fever. The convulsions were repeated and back and neck became rigid, the bowels were constipated, there was no cough or vomiting on day of admission to hospital.

Physical Examination. By house physician: General condition, fair; patient well nourished; slight soporous condition; continues to lie on the left side; irritable; there is moderate rigidity of the neck. Marked MacEwen; slight Kernig; tache cerebrale. Patient can be aroused from soporous condition; does not seem to be conscious but simply moans and cries; respiration somewhat irregular; cheeks flushed; puts hands to head at times; twitching; no retraction of the head. The skin shows some flea-bites "tache bleuatre," no petechiæ; ears and mastoid negative; pupils regular; central easily dilated; conjunctivæ injected; no paralyses; there are sordes in mouth; teeth and gums in good condition; tongue is coated and moist; throat shows mucó-pus; no facial paralysis; thyroids and spine negative; few small axillary and inguinal glands to be felt; chest negative, somewhat sunken; abdomen retracted; liver, spleen, genitals negative. Extremities: slight edema over the tibiæ, knee-jerks not obtained, no Babinski, no paralyses.

Synopsis. Stupor, MacEwen, Kernig, rigidity of the neck, tache cerebrale.

February 9. Lumbar puncture, 35 cm. of clear fluid removed under great pressure, and 30 cm. of Flexner serum injected as a precaution should meningococcus be present on examination. White blood cells, 72,000; polynuclears, 79 per cent.; Cutaneous tuberculin reaction, negative.

February 10. Patient lies in a crouched position; is irritable when disturbed; cries out and is exceedingly hyperæsthetic; retraction of head; rigidity; Kernig, as yesterday; arms and extremities; some edema still present today, patients has ordinary redness of fauces; chest negative; patient does not take nourishment.

February 11. Has a general erythematous rash (serum); patient lies in same position as yesterday, general condition about the same; delirious when disturbed; rigidity and Kernig still present. Today, the nurse reports she sat up and took notice of things.

February 12. Patient much improved, opens her eyes and seems to notice objects; is much clearer and does not resist quite so much. There is still very marked Kernig and very marked rigidity of the neck and retraction of head; there is mydriasis when head is flexed, slight strabismus on left side.

February 13. When patient was admitted the urine was of a distinctly brownish tint, today it is clear but distinctly colored. Estimate of urine very difficult on account of the involuntary discharges. Patient when left alone very quiet, when interfered with still resists, does not answer questions. Patient seems to be more conscious, but apparently deaf; no paralyses; Kernig still present.

White blood cells; 12,000; polynuclears, 83 per cent.; fundus of the eyes normal.

February 14. Patient last night sat up, was quite logical but apparently deaf; when any one approaches her the patient is frightened, but much more rational than yesterday; no edema of the tibiae. There is Kernig; rigidity of neck; no MacEwen, excretions involuntary.

February 15. Patient hears; more rational; has right external strabismus, this was noted yesterday; rigidity of neck still present, as also Kernig; has normal reflexes on both sides; some edema of the tibiae.

February 16. Patient improved, more rational; Kernig and rigidity still present; the urine is normal.

February 17. Patient sits up; quite rational; external strabismus of the right eye unchanged; Kernig still present; headache yesterday, none today.

February 19. Continues to improve; no apparent paralyses of the extremities; no paralysis of facial muscles.

February 22. Complains of lack of power of left hand, right grasp is little stronger; no limitation of motion of upper extremities no apparent atrophy.

February 24. Slight limp in left leg; knee-jerks on left side diminished.

February 25. Patient looks bright; feels well; slight Kernig; slight weakness of left upper extremity.

March 2. Patient examined today, appears bright and normal; slight loss of power in left hand; no atrophy of muscles visible in upper and lower extremities; no loss of power; no Kernig; no Babinski; no ocular or facial paralyses. Patient has loss of power in left arm, but more apparent than real.

The temperature of patient from admission, February 8 to February 14, ranged from 104°, gradually fell on February 14 to 100°; respiration pretty regular from 22 to 32; pulse from 90 to 120. The following days temperature, pulse, and respiration were normal.

The night nurse reports that on admission and on days after the child was particularly noisy at night at intervals. During the day, was quite comfortable. The urination was almost always involuntary. She refused nourishment, was constipated up to February 12, after which time she slept at night and was quiet. The puncture fluid was reported as practically normal; there was sugar present, also traces of albumin; cytological examination showed a few mononuclear cells. Wassermann was negative. The urine was catheterized, and, with the exception of a few bacterial cells, was sterile.

Examination of Urine. February 11. Hyaline and granular casts, and some blood and pus.

February 12. About the same, blood, pus, and casts.

February 14. A few granular casts.

February 15. No casts and no blood, and negative after that time with the exception of a few leukocytes.

DISCUSSION. In this case the onset was acute, there then was a remission in symptoms and then the patient took to bed after a week with all the symptoms of a meningitic attack; in fact, when seen in consultation, a cerebrospinal meningitis was suspected, and a puncture was made with that diagnosis in view, but the fluid obtained was clear and nothing found but a lymphocytic cytology. There was a high leukocyte count of the blood, including an excess of polynuclear cells. The illness ran the course of an acute meningitis. The find in the urine corresponds to that found by Wickman in one of his cases, inasmuch as the urine cleared up completely, it must be surmised that the nephritis was only part of a general infection. The patient fully recovered with a strabismus due to ocular palsy remaining with slight weakness in the left upper extremity. This, I think, is a case of acute polioencephalitis with a meningitic onset, its course closely simulating cerebrospinal meningitis of the epidemic type. The patient was not discharged until she had absolutely recovered.

CASE V.—Female, aged five years. Admitted October 14, 1909.

Family History. Father suffering from pulmonary tuberculosis. Mother and nine other children healthy.

Previous History. Full term; no instruments. History of measles at two and one-half years, no complications. Whooping cough just previous to measles. Has had a dry moderate cough since having measles up to one year ago. No convulsions; no ear symptoms; bowels regular; urination normal. About sixteen months before admission, patient was operated for acute appendicitis. Ill five weeks. Healthy since, until present illness.

Present illness began four days ago when mother noticed that child became drowsy, lost interest in surroundings and developed moderate fever. On day after onset, child vomited for the first time. Vomitus consisted at first of undigested food, later of small amounts of bile stained fluid, accompanied by much retching. Has been vomiting since, chiefly after taking of food.

Since onset, bowels are obstinately costive. No marked abdominal distention, no blood or mucus in stool. Drowsiness has become intensified, child starts in her sleep with a shriek. Sighs considerably. Day before admission, child complained of pain in back of neck, developed some rigidity and has become delirious and irrational. No convulsions; no palsies; slight dry cough; no dyspnea. Marked prostration; drowsy; responds when disturbed; is irrational and delirious. Respiration irregular, no head retraction; neck is rigid. General hyperesthesia, MacEwen present, especially on left side; marked photophobia.

Eyes, ears, and mastoids, are normal.

Skin, scar of operation; tache cerebrale present; scattered papular spots.

Lymph nodes, few small left axillary.

Tongue, dry and coated. Throat, teeth, and gums good condition. Chest well formed; lungs clear; heart borders normal; action regular, rapid, poor force, sounds clear, no murmurs.

Pulses, equal, regular, rapid, small.

Liver and spleen, not enlarged. Abdomen lax, reflexes present.

Extremities, Kernig's present, held somewhat stiffly. Slight Kernig on left side; left Babinski at times.

Synopsis. Fever, drowsiness, delirium, hyperesthesia, rigidity of neck, MacEwen, left Kernig.

Blood Count. White blood corpuscles, 21,000; polynuclears, 61 per cent.; small lymphocytes, 28 per cent.; large lymphocytes, 11 per cent.

October 15. Lumbar puncture, 24 c.c. clear, colorless fluid under increased tension withdrawn.

October 16. This A.M., is semi-conscious, rouses when talked to; athetosis in hand, dry-coated tongue; talks with lisp; slight flatness of left side of face; Kernig on both sides; marked rigidity and tenderness of neck; slight MacEwen on left side.

October 17. Lungs negative; paresis left side of face more marked; marked rigidity of neck; marked Kernig on both sides. Fundus examination of eyes negative. Patient semi-conscious. Von Pirquet positive.

October 18. More conscious; Kernig left facial; MacEwen very slight on left side, slight internal rotation of left eye; marked neck rigidity.

October 23. Von Pirquet still evident; Kernig; left facial flatness; bromide eruption on legs. Can sit up; rigidity at neck almost gone; tongue moist; MacEwen not elicited.

October 25. Sitting up; left side of face still slightly flat; neck supple; Kernig 30° on both sides.

Urine. October 24. Amber, acid; specific gravity, 12; albumin 0; few white blood corpuscles.

November 4. Amber, acid; specific gravity, 24; albumin 0; few white blood corpuscles.

October 15. Cerebrospinal fluid—cytology lymphocytes, 100 per cent. Negative for bacteria; no growth; no tuberculosis. Albumin, $\frac{1}{2}$ mm.; sugar reducing substance present. Widal negative, 1 to 20, 1 to 50, also on October 18.

October 14. Temperature 104.2° on admission, dropped to 100.8° on following day, and on October 16 reached 99°; slight rises to 100° since. Pulse 116 on admission, respiration 28. Weight 45 $\frac{3}{4}$ pounds.

DISCUSSION. This patient, five years of age, was attacked more or less acutely with high fever and vomiting, passed into a condition

of sopor which became intensified after a few days. There was the picture of meningitis with fever, drowsiness, delirium, apathy, vomiting, constipation, pain in neck and rigidity of the neck. What was especially disquieting, was a positive Von Pirquet cutaneous reaction to tuberculin, which misled into the diagnosis of tuberculous meningitis. The subsequent complete recovery disproved this, leaving us to infer a latent glandular tuberculosis. The fluid obtained by lumbar puncture showed nothing more than a marked lymphocytosis.

The recovery in this case was complete, there being left only a slight facial flatness, no real paralysis. The temperature after the first day after admission to the hospital was normal. The urine was normal; the fundus oculi was normal.

CASE VI.—This case resembles a case I saw recently in consultation, a girl, aged thirteen years. The case was seen by several physicians, all being quite positive in the diagnosis of tuberculous meningitis. This girl, like the case I am to depict has recovered with the exception that she did not, as this case, yield positive tuberculin skin reaction.

This case was a boy, aged four years, admitted to my hospital service. Had had measles, scarlet fever, and diphtheria.

Present illness began three weeks ago with an attack of fever and vomiting, headache following this, the boy became drowsy, did not notice and was soporous and stupid. The condition of drowsiness became more and more marked, and in this condition he was brought to the physician. The patient was well nourished, had some slight hydrocephalus, staggered when upright, swayed especially to the left when he walked and threatened to fall. The patient was in a trance-like state and sat up in bed staring ahead; slept well. The examination of the fundus oculi was negative.

The patient's urine at first contained acetone, diacetic acid, and a trace of sugar. These disappeared in the first two days of the hospital stay. After three weeks of illness the above symptoms cleared and the patient was well. There was from the first, a positive tuberculin skin reaction (Von Pirquet). No lumbar puncture was made. This case differs from that of the girl I just mentioned, inasmuch as the latter had no tuberculin reaction, was unable to sit up or stand without experiencing marked vertigo. The girl was extremely hyperesthetic, whereas this symptom was absent in the boy.

I have thus described a condition which is of great interest. It is apt and is constantly mistaken for meningitis of the cerebro-spinal acute suppurative or subacute tuberculous form. The onset of the illness is acute; it begins with a previous history of absolute health. After the acute symptoms set in, there may be in some cases an abatement and then a recurrence of symptoms of a cerebral nature, which gradually deepen. If the case is one resembling an

acute meningitis, the symptoms are more active with neck rigidity, pain in the neck, headache, and delirium. If the case resembles the tuberculous forms of meningitis, the patient lies more quiet. Exhibits palsies of the cranial nerves, and may even have marked hydrocephalus with distinct Cheyne-Stokes respiration and unconsciousness. In both sets of cases the delirium, sopor, or coma lightens the patients after a week or more of illness becoming brighter, and recovery proceeds. Lumbar puncture in all the cases reveals a clear or slightly flocculent fluid, without bacteria, and a cytology of 90 per cent. to 100 per cent. lymphocytes. An examination of the blood shows a leukocytosis at first of pronounced degree of polynuclear type.

The onset of the disease may be ushered in by fever, which rapidly subsides to within a fraction of a degree of the normal and the major part of the illness runs its course with this temperature, which is practically normal. The diagnosis is made from the points of clinical course laid down in this paper. The prognosis is for the most part good, except in those cases which involve the nuclei of the nerves controlling respiration. In such cases the outlook is that of an acute bulbar paralysis where the extent of the lesion will decide the fate of the case. The main point is to have in mind the great similarity of a certain set of these cases to those of tuberculous meningitis, and the absolute futility of a positive diagnosis without study of the case, lumbar puncture and all the clinical aids at our command.

ABSCESS OF THE LIVER OCCURRING IN ASSOCIATION WITH OR FOLLOWING TYPHOID FEVER.

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THE occurrence of suppurative processes in the liver during the course of or following typhoid fever has been recognized since the time of Louis. In recent years papers by Romberg, Osler, Sheldon, and Cassuto, and at the beginning of the present year an exhaustive study of the subject by Melehior of Breslau, have appeared.

Abscess of the liver occurring in association with or following typhoid fever may be either multiple or solitary. Romberg in 1890 ascribed the formation of these liver abscesses to the following causes: (1) Typhoid ulceration of the gall passages proceeding to suppuration; (2) suppurative pyelephlebitis in association with typhoid fever; (3) pyemic infection from some other point in the body. This classification of the precursory lesions of abscess

of the liver, though still generally adhered to, is too restricted. Abscess formation may occur at the site of focal necrosis, infarction, or injury, or in association with preëxisting disease, or possibly from undetermined causes.

Of these suppurative lesions solitary abscess has come to be considered an important clinical type, as in such cases only may surgical treatment be undertaken with prospects of success. It is with this type of abscess that I wish to deal.

The general *résumé* here submitted is founded upon a critical examination of the reports of 30 cases. These cases are divided into two groups, the first including those in which the presence of *Bacillus typhosus* as an etiological factor was confirmed by bacteriological examination—the second, those cases in which abscess occurred in association with or following typhoid infection, but in which *Bacillus typhosus* was not isolated.

INCIDENCE OF ABSCESS OF THE LIVER OCCURRING IN ASSOCIATION WITH OR FOLLOWING TYPHOID FEVER. There are no satisfactory data upon this point. The statistics available include cases of suppuration in the liver secondary to typhoid infections of the gall passages and the portal system, in which two conditions, as one would expect, multiple foci of suppuration are almost invariably found postmortem. In Hölscher's statistics of autopsies made at the Pathological Institute of Munich on 2000 fatal cases of typhoid fever, 12 cases of liver abscess are included. Romberg collected 677 cases of typhoid with 88 deaths, among which there was 1 case of liver abscess; Dopfer—927 cases, with 10 cases of abscess of the liver. There is also the interesting report from New Caledonia by Legrand of the occurrence of 6 cases of abscess of the liver in 133 consecutive cases of typhoid fever.

AGE AND SEX. In the collected cases the age varied between five and forty-three years. There were in the first decade 4 cases; in the second, 2; in the third, 19; in the fourth, 4; and in the fifth, 1. There were 22 males and 8 females.

PREDISPOSING FACTORS. (a) *Virulence of the primary infection.* Solitary abscess is generally the sequel of a mild type of infection. This may possibly be partially explained on the basis of the development in such cases of an incomplete immunity. Of the severe

TABLE I.

Severe cases: Nos. VI, VIII, XI, XIV, XXVI, XXVIII	= 6
Moderately severe: Nos. II, IV, V	= 3
Mild: Nos. I, III, VII, IX, XII, XIII, XV, XVI, XVII, XVIII, XXVII, XXIX, XXX	= 13
Not classified: Nos. X, XIX, XX, XXI, XXII, XXIII, XXIV, XXV	= 8

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infections Cases VI, VIII, XXVI, and XXVIII were characterized by intestinal hemorrhages. In Case VIII there occurred also

thrombosis of the vena saphena parva, and in Case XXVIII the onset of the illness was marked by vomiting and complicated by the presence of pleuritis. In Case XI severe diarrhoea occurred during the course of the illness. Vomiting and abdominal pain were the initial symptoms of the primary infection in Case XIV. In the moderately severe cases no complications occurred previous to the onset of the symptoms of liver abscess. The same remark applies to the unclassified group of 8 cases. In this group, however, the case reports with the exception of Case X are completely lacking in detail. Of the mild infections the symptoms of abscess in Case III followed a relapse; in Case VII the infection was of the ambulatory type. In Case XII numerous subcutaneous abscesses developed concurrently with the involvement of the liver; all of these, however, underwent spontaneous resolution.

(b) *Traumatism.* The case of Sennert (VII), in which a typhoid infection following injury led to suppuration in an involuting hematoma of the liver, establishes the possible role of traumatism.

(c) *Preëxisting disease of the liver* may determine the occurrence of typhoid abscess formation. The case of Hühn and Joanovic (V) of secondary infection of an echinococcus cyst of the liver by bacillus typhosus is cited in detail. The case of Caton and Thomas (XXVII) is presumably of the same nature.

TABLE II.

New Caledonia, Java, Ile Nou: Cases XV, XVI, XVII, XIX, XX, XXI, XXII, XXIII, XXIV	= 9
North Africa: Cases II, XIII	= 2
China: Cases IV, XXIX	= 2
Southern States: Cases XXVI, XXVIII.	= 2
Northern Europe, Northern States and Canada: Cases I, III, V, VI, VII, VIII, IX, X, XI, XII, XIV, XVIII, XXV, XXVII, XXX.	= 15
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(d) *Climate.* There appears to be no ground for considering climate a predisposing factor. While it is true that of the 30 cases reviewed, 15 occurred in tropical or subtropical lands, in only 3 of these cases (II, IV, XXVIII), are the bacteriological reports adequate. In Wendel's case (XXIX), cultures were negative, but it is stated that amoebic infection cannot be excluded. In the remaining 11 cases no bacteriological reports are given. Of the 13 cases reported from Africa, China, and the Antipodes, 10 were in soldiers, who are more than other individuals exposed to typhoid and amoebic infection. In the 15 cases reported from Northern lands bacteriological reports are lacking in only 5 instances, all of which occurred prior to 1888. In the remaining 10 cases the typhoid bacillus was identified in 9 instances and the colon bacillus in 1.

While the above analysis would seem to exclude the influence of climate as an exciting factor, the possibility of a double infection

should be borne in mind, especially in districts where amœbic dysentery is prevalent. A case reported by Wendel may be cited in illustration: An adult male was admitted to the Military Hospital at Shanghai, June 10, 1902, suffering from a moderately severe typhoid infection. During convalescence the patient developed dysentery. In August he had pain in the region of the liver radiating to the right shoulder; dulness and a pleuritic friction were present at the right base; there was an evening rise of temperature. August 8, exploratory puncture in the right axillary line withdrew pus. This procedure was followed by the transpleural evacuation of an abscess the size of a goose egg, situated in the dome of the liver. No bacteriological examination of the discharges was made. The patient recovered.

In Cases IV and XXIX a double infection is not excluded.

Open typhoid lesions of the bowel may predispose to secondary amœbic infection and indirectly to amœbic abscess of the liver in the presence of or without the existence of typhoid lesions, such as focal necroses, in that organ. How far in double infections the presence of bacillus typhosus promotes the growth of amœbæ is an interesting speculation in the light of the cultural experiments of Musgrave and Clegg.

Even in Northern latitudes typhoid and amœbic infections may co-exist. Within the past year an instance of fatal amœbic infection of the liver occurring in an individual who had never been outside of Canada has been reported from the Province of Quebec.

FEVER-FREE INTERVAL. A perusal of the cases here reviewed yields the fact that in 7 instances no fever-free interval occurred. In 13 cases there was a definite afebrile period varying from two days to one year, while in 6 cases symptoms of abscess are stated to have appeared "during convalescence." In the reports of 4 cases no reference to an afebrile period is made. For details one should refer to the following table:

TABLE III.

No interval: Cases I, II, III, IX, XIII, XXVIII, XXX	= 7
Fever-free interval of 2 days, Case XII	
6 days, Case VIII	
14 days, Cases V, X, XVIII, XXIV	
18 days, Case XXIX	
19 days, Case XXVII	
21 days, Case XV	
27 days, Case IV	
1 month, Case XXIII	
3 months, Case XXVI	
1 year, Case XXV	= 13
"During convalescence:" Cases XVI, XVII, XIX, XX, XXI, XXII.	= 6
No reference to fever-free interval: Cases VI, VII, XI, XIV	= 4

The time of onset of the symptoms of abscess in relation to that of the primary infection is set forth in the following table, the time being stated in the "week" of the disease—the "day" also being given in those cases in which the onset of the complication was unusually early:

TABLE IV.

Second week: Case XIII (thirteenth day); XXVIII (eighth day).	= 2
Third week: Case XXX (nineteenth day)	= 1
Fourth week: Case IX (day uncertain); XVIII (twenty-eighth day).	= 2
Fifth week: Case I (thirtieth day); VI (day uncertain); VII (day uncertain); XII (thirty-second day)	= 4
Seventh week: Cases XV, XVII, XXVII, XXIX	= 4
Eighth week: Cases II, III, V	= 3
Ninth week: Cases IV, VIII	= 2
Three months: Cases XI, XXVI.	= 2
One year: Case XXV	= 1
Not computed: Cases X, XIV, XXIII, XXIV	= 4
During convalescence: Cases XVI, XIX, XX, XXI, XXII	= 5

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Those individuals in whom liver abscess develops after a prolonged post-typhoid afebrile interval may possibly be typhoid carriers.

GENERAL SYMPTOMATOLOGY. The most characteristic symptoms of onset were pain in the right hypochondrium or epigastric region, temperature of a septic type, and either enlargement of the liver or the detection of a mass in association therewith.

Enlargement of the liver was noted to be present in 22 cases; was obscured by the presence of adhesions in one instance; and in 7 cases (including 6 reported by Legrand) details are lacking but from the postmortem findings enlargement may be assumed to have been present. Pain as an initial symptom is stated to have been absent in only 3 cases; in 2 of these (I and III), the patients were only five years of age, and in the third (XXVII) suppuration took place in a preëxisting lesion, possibly an echinococcus cyst. This absence of pain in children may be accounted for by the greater distensibility of the tissues, especially the overlying thoracic structures. Initial vomiting occurred only five times. In 1 case nausea was noted. Chills were noted in 8 instances, and chilly sensations in 2. Chills are definitely stated to have been absent in 2 cases. This symptom is considered more fully later. Jaundice is usually absent, having been present in a well-marked form in only 4 cases of the series.

Thus, of the symptoms of onset, enlargement of the liver is undoubtedly the most constant and the most characteristic. The increase in the area of liver dulness may be upward when the lesion is situated in the dome of the liver, or downward when the left lobe is involved or the focus of suppuration is situated toward the anterior surface. Enlargement may be confined to one lobe.

In the case of McCrac and Mitchell there was made out an indefinite mass associated with the liver. The formation of adhesions, as in Case XIII, may obscure the physical signs of enlargement. Suppuration beneath the capsule of the liver, leading to local peritonitis or perihepatic abscess, gives rise to more marked pain than deep-seated lesions, and is associated with rigidity and muscular spasm. Where the lesion is situated in the dome, extension of the range of liver dulness may be entirely upward; more often, however, it is in both directions. These cases are not infrequently associated with the formation of pleural effusion, either serous or purulent; more rarely rupture into the pleural cavity occurs.

Position of the abscess.

TABLE V.

Right lobe: Cases II, IV, VII, VIII, IX, XIV, XV, XVI, XVIII, XX, XXI, XXIII, XXVI, XXVIII, XXIX, XXX	= 16
Left lobe: Cases I, III, XIII, XIX	= 4
Whole liver: Cases XVII, XXII, XXIV.	= 3
Not definitely reported: Cases V, VI, X, XI, XII, XXVII	= 6
Subdiaphragmatic: Case XXV	= 1
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Secondary perihepatic collections of pus were present in Cases VIII and XXVIII. In Case IX there was a general peritonitis and free communication between the abscess and the abdominal cavity. In these 3 cases the presence of muscular spasm attested to the peritoneal involvement.

Chills.

TABLE VI.

Chills were noted in Cases III, VIII, IX, X, XII, XXV, XXVI, XXVII	= 8
Chilly sensations were noted in Cases XI, XVIII.	= 2
Chills were absent in Cases I, VI	= 2
Chills were not mentioned in Cases II, IV, V, VII, XIII, XIV, XV, XVI, XVII, XIX, XX, XXI, XXII, XXIII, XXIV, XXVIII, XXIX, XXX	= 18
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It should be noted that chills occurred in 3 of the cases (VIII, IX, and XXVII) from which typhoid bacilli were isolated in pure culture, whereas in Case VI, in which streptococci were found in association with typhoid bacilli, chills are stated to have been absent throughout the illness.

Jaundice. The number of cases in which well-defined jaundice developed is surprisingly few, such cases being Nos. V, VII, XII, and XXVIII. Case XI is described as "sallow" and Case XVIII, as having subicteroid discoloration of the skin. Jaundice is definitely stated to have been absent in Cases I, IV, VI, IX, XXVI, and XXIX, while there is no mention of this symptom in Cases II, III, VIII, X, XIII, XIV, XV, XVI, XVII, XIX, XX, XXI, XXII, XXIII, XXIV, XXV, XXVII, and XXX, a total of 18

cases. The autopsy notes on Cases XIII and XIV state that the bile passages were normal. The 6 cases reported by Legrand (XIX, XX, XXI, XXII, XXIII, and XIV), are lacking in all detail. Of the other cases, however, we have fuller reports and it is reasonable to assume that jaundice was absent. These observations tally generally with those of Da Costa.

Multiple Foci of Suppuration. In Case XXI there were multiple foci of suppuration, that is, in addition to the large abscess in the right lobe there were two small abscesses in the left lobe. This finding is especially interesting when viewed in comparison with Case XIX, reported by the same author, in which there was found a "cicatrized" abscess in addition to the active lesion from which the patient died.

Cases IX and XIX should be considered in conjunction with Case XII, in which numerous subcutaneous foci of suppuration underwent resolution without surgical interference. These definite and varied indications of a tendency to resolution in the suppurative lesions of typhoid may explain the halting character of the initial symptoms of abscess in certain cases and may also explain those cases which have been met with during defervescence or convalescence in which symptoms of enlargement of the liver with pain and tenderness—not suggestive of cholecystitis—gradually subside. This suggestion might be challenged on the ground of the infrequent occurrence of postmortem evidence of healed abscess in the liver. These abscesses, however, are probably small; the regenerative powers of the liver cell are known to be very great; and, further, the vast majority of cases of typhoid occur in the third decade or earlier and do not, under the normal prospect of life, come to autopsy for many years, if ever.

ASSOCIATED COMPLICATIONS. (a) *Peritonitis*. In Case IX peritonitis followed rupture of the hepatic abscess and although five days elapsed before drainage was established, the patient made an uneventful recovery. In this case the cultures yielded a pure growth of typhoid bacilli, and it is quite conceivable that complete resolution of such a peritonitis might have taken place without the establishment of drainage. Peritonitis was the terminal condition in Cases XIII and XVII.

(b) *Pleuritis* occurred as an associated complication in 7 cases—serous or serofibrinous in Cases XIV, XXVIII, and XXIX, and purulent in Cases II, X, XV, and XXV. In Cases X and XV the pleural collection communicated directly with the abscess cavity through an opening in the diaphragm.

BACTERIOLOGY. Bacteriological reports are furnished in connection with 14 of the cases. In 7 instances (I, II, V, VII, VIII, IX, XXVII), typhoid bacilli were isolated in pure culture, and in 4 other cases, in association with staphylococci or streptococci (III, IV, VI, XXV). In 1 case (XXX) *bacillus coli communis* was

apparently the etiological factor. In 2 cases (XXVIII, and XXIX), cultures taken at the time of operation were negative; in Case XXVIII careful search was also made for amœbæ. This latter case suggests that, just as in pyothorax following diplococcus pneumonia, the infecting organism may entirely die out by the time drainage is effected. Not only may all the organisms be dead but bacteriolysis, so rapid in the case of bacillus typhosus, prevents the determination of their presence even in coverslip preparations. Wendel states that in his case (XXIX) he is unable absolutely to exclude amœbic infection.

TREATMENT AND TERMINATIONS. Of the methods of treatment that of puncture or aspiration has been the most fatal. Of 6 cases treated by puncture all succumbed. Case XI, also treated by this method, frequently repeated, finally came to a successful issue through rupture of the abscess into the bowel. Of the 3 cases in which spontaneous drainage was effected through rupture into the bowel, Case XXIV alone succumbed. The course of Case X is of extreme interest as at the first illness evacuation of the abscess contents occurred through a bronchus, and at the second (one year later) the abscess evidently burrowed downward within the abdominal wall and ruptured externally near the right anterior superior spine. Laparotomy and drainage was carried out in 9 cases—the one fatality occurring in Case VI, in which there was abundant ascites at the time of operation. As a chain coccus was found in association with the typhoid bacillus, it is probable that death ensued from peritonitis. Drainage by the transpleural route was effected with satisfactory results in 5 cases. In Case II, that of Remlinger, operative interference was directed solely against the empyema, no connection existing between the hepatic and the intrapleural collections of pus. The 4 untreated cases died—Cases XIII and XVII from peritonitis. In Case XIV the liver condition was complicated by a right-sided serofibrinous pleuritis, and in Case XV the abscess in the liver communicated through a perforation in the diaphragm with the right pleural cavity.

TABLE VII.

	Died.	Recovered.
Puncture: Cases XI, XVI, XIX, XX, XXI, XXIII, XXVI	6	1
Rupture into bowel: Cases XI, XII, XXIV	1	2
Rupture into bronchus: Case X		1
Rupture iliac fossa: Case X		1
Laparotomy and drainage: Cases I, III, V, VI, VIII, IX, XXV, XXVIII, XXX	1	8
Thoracotomy and incision of diaphragm: Cases IV, VII, XVIII, XXVII, XXIX		5
Thoracotomy: Case II	1	
Not treated: Cases XIII, XIV, XV, XVII, XXII	5	
	<hr/> 14	<hr/> 18

N. B. Cases X and XI each appear under two headings.

From personal observations I am convinced that the employment of preliminary diagnostic puncture of the liver by the transperitoneal route exposes the patient to the danger of peritonitis. Even in deep-seated abscess the pus, always under tension, will escape along the path of a fine needle wound. The clinical report in Case VI suggests that peritoneal infection followed exploratory puncture. The risk of empyema following transpleural puncture of the liver is relatively less owing to the interposition of the diaphragm; furthermore, empyema is fraught with much less danger to life.

The danger of disseminated echinococcus infection of the peritoneal cavity following exploratory puncture has long been recognized.

CONCLUSIONS. 1. That abscess of the liver occurring as a complication or sequel of typhoid fever may arise independently of typhoid lesions of the gall-bladder or ducts, pyelephlebitis, or the presence of suppuration elsewhere in the body.

2. That the recognition of solitary abscess is important because of the fact that only such cases are suitable for surgical treatment.

3. That age and sex have no bearing upon the incidence of liver abscess apart from their relation to typhoid fever generally.

4. That as predisposing factors, the virulence of the primary infection, traumatism, and preëxisting disease would appear to have been established.

5. That the frequency of liver abscess in relation to typhoid fever reported from hot climates may be accounted for (*a*) by the high incidence of typhoid infection in European drafts, and (*b*) by the preëxistence or occurrence during convalescence of amœbic infection.

6. That the onset of the symptoms of liver abscess may occur early in the course of the primary infection, after a fever-free interval of days or weeks, or as a remote sequel. The relation of typhoid carriers to the last class is a subject for further investigation.

7. That of the symptoms of onset enlargement of the liver, fever, local pain, and tenderness, are the most characteristic.

8. That jaundice is present in about 15 per cent. of the cases only.

9. That in about 50 per cent. of the cases the focus of suppuration is located in the right hepatic lobe.

10. That the occurrence of chills is apparently without relation to the organism or organisms found in the local lesion.

11. That there would appear to be ground for the assumption that foci of suppuration in the liver due to bacillus typhosus may occasionally undergo spontaneous resolution.

12. That pleuritis, either serous or purulent, not infrequently occurs as an associated complication.

13. That the only safe method of treatment is by incision and drainage—the route selected, either abdominal, or transpleural, depending upon the location of the abscess. Preliminary transperitoneal puncture should not be practised owing to the danger of leakage and peritonitis.

14. That in future observations upon such cases the scope of the bacteriological investigations should include the use of media especially suitable for the cultivation of *Bacillus typhosus*, as well as careful search for amœbæ.

Group I.

CASE I.—Author's Case. The salient features of this case were: (1) The absence of the usual fever-free interval; (2) the rapid progress of the local lesion without the occurrence of intervals of improvement; (3) the pronounced character of the constitutional symptoms—fever, prostration, anæmia, high pulse rate; (4) the absence of local signs apart from enlargement of the liver; (5) the absence of the following symptoms: pain, either local or radiating to the shoulder, local tenderness, jaundice, chills, sweating, and vomiting; (6) the escape of the whole of the biliary secretion through the operation wound owing to obstruction of the common duct, presumably by blood clot, fibrin or detritus from the abscess cavity, associated with clay-colored stools; (7) the arrest of pancreatic digestion and the escape of pancreatic juice through the operation wound; (8) the relief of the two latter conditions by raising the tension within the biliary passages; (9) the direct growth from the abscess contents of *Bacillus typhosus* in pure culture; (10) recovery.

A. A., a girl, aged five years and five months, was taken ill September 8, 1905. On September 16 (ninth day) the diagnosis of typhoid fever was confirmed by the presence of rose spots and the positive agglutination reaction in dilutions of one in eighty. The spleen was enlarged. The accompanying chart shows the daily temperature range from the fastigium until the establishment of convalescence. Toward the end of the second week the liver was palpable below the costal margin at the tip of the ninth rib. Throughout the illness the bowels were constipated. Nourishment was well taken. Owing to the tender age of the patient, tepid spongings were given instead of baths.

The alteration in the temperature curve on October 7 (thirtieth day), and its gradually increasing range during the following week, was looked upon as a recrudescence. The spleen showed progressive enlargement. No new rose spots appeared. The patient's

only complaint was of hunger. At this time, also, there was noted a slight increase in the liver dulness in the median line, but palpation failed to reveal the presence of tenderness either in this region or in that of the gall-bladder. There were no complaints of pain on deep inspiration, or when the patient's position was changed. The lungs were normal. The urine contained a trace of albumin and a few granular casts. The reaction for bile was absent. There was no jaundice. Although nourishment was well taken, the patient continued to lose weight and the mucous membranes and pinnæ showed a rapidly increasing anemia.

From the thirty-fourth day onward there was noted in the epigastric region a progressive increase in the area of hepatic dulness. There was, however, no complaint of pain. Muscular spasm and even the sense of resistance was entirely absent. Firm pressure over the left lobe of the liver failed to elicit tenderness. There was no evidence of an increase in the area of the liver dulness in an upward direction. There were neither chills, chilly sensations, nor sweating; but owing to the character of the temperature curve and the progressive enlargement of the liver, abscess of the left lobe was diagnosticated. On the evening of the forty-sixth day the fulness in the epigastrium had become very pronounced, and for the first time the patient complained of pain along the right subcostal border upon being turned in bed. There was also detected distinct tenderness on pressure in the median line midway between the umbilicus and the ensiform cartilage.

The patient was prepared for operation in her own home on the morning of the forty-seventh day. Under chloroform anesthesia the left lobe of the liver was exposed and the capsule found to be free from adhesions or exudate. The lower margin extended to the level of the umbilicus. The liver appeared normal in color. On palpation a deep area of tension was detected. An exploratory puncture at this point yielded pus. A grooved director was then passed along the course of the needle and the path to the abscess cavity dilated by means of hemostatic forceps. From one to two ounces of grayish odorless pus escaped, followed by a fairly free hemorrhage. So far as could be judged from the use of the director, the cavity (about 5 cm. in diameter) lay well within the substance of the left lobe of the liver. A drainage tube was placed in position.

Cultures taken at the time of operation showed at the end of twenty-four hours the following: On agar slants a heavy growth of dull white colonies which in cover glass preparations showed only bacilli with oval ends, decolorizing by Gram's stain. Stab cultures in peptone gelatin showed on the surface a growth spreading from the puncture as a thin film, bluish-white in color, and along the stab an opaque whitish line, without liquefaction of the medium or the formation of gas. Bouillon at the end of the same period showed a uniform turbidity, the organism, in addition to

the morphology described, appearing in filaments. In litmus milk there was no coagulation of the casein.

Hanging drop preparations from bouillon culture showed actively motile bacilli, which were rapidly agglutinated by a one-in-two-hundred dilution of the blood serum of a typhoid patient giving at the same time a positive Widal reaction with laboratory cultures of *Bacillus typhosus*.

All cultures were free from cocci or other contaminating organisms. (Transplants from the bouillon culture were subsequently used in the laboratory for routine Widal reactions.)

The dressings, when changed at 10 P.M. on the day of the operation, were deeply bile-stained.

October 27. Chloroform was administered to change the packing and the tube. An enema resulted in the passage of a large, clay-colored stool. It was evident that the operation had established a communication between the abscess cavity or drainage tract and an important branch of, if not the main biliary duct of the left lobe of the liver. The absence of bile in the stool was assumed to be due to a blockage of the common bile duct with blood clot and detritus.

Subsequently the dressings, changed twice daily, continued to be deeply bile-stained. The improvement in the patient's general condition was marked.

November 6. The discharge from the wound became profuse, watery, and less deeply bile-stained, necessitating the changing of the dressings four times during the twenty-four hours. The pulse was irregular. The stools were large, colorless, very offensive, and fatty. The general condition of the patient was less satisfactory. The temperature remained constantly subnormal.

November 7. The profuse discharge from the wound continued. The pulse at times became very rapid and irregular. The patient was apparently losing weight rapidly. Ox bile, pepsin, and essence of diazyme were administered with the nourishment.

November 8. The discharge was more profuse and watery, saturating six large dressings in twenty-four hours, with the escape of fluid on either flank. The wasting was rapid and the prostration profound. There was marked pallor and restlessness. The stools remained clay-colored, and were large and fatty. The general condition of the patient was critical.

Although nourishment was well taken and in sufficient quantity it was evident that some profound nutritional disturbance was present. Reverting to the hypothesis advanced to account for the absence of bile in the stools, it was assumed that the sudden increase of discharge associated with arrest of pancreatic digestion and failure of nutrition might be due to the downward displacement of the fibrinous residue of the clot occupying the common duct and its impaction in the ampulla of Vater, or at a point below

the junction of the canal of Wirsung and the ductus communis choledochus. This hypothesis would account not only for the nature of the stools but also for the presence of the profuse discharge (pancreatic). It became imperative to try the effect of raising the tension in the biliary passages as a means of overcoming the obstruction. To this end, on the morning of November 9, under light anesthesia, a firm gauze packing was inserted along the path of the drainage tube.

November 10. A soap-suds enema at 7 A.M. resulted in the passage of a liquid stool, distinctly bile-stained. The general condition of the patient had improved greatly and there was a marked decrease in the pulse rate.

From November 11 convalescence was uninterrupted.

At the time of writing five years have elapsed and the patient is in excellent health.

CASE II.—Remlinger. A cavalryman, aged twenty-one years, was admitted to hospital November 21, 1896. The diagnosis of typhoid fever was confirmed by the presence of a positive serum reaction. The infection was rather more severe than the average. January 12 (about the fiftieth day) the patient complained of localized pain over the liver, which, however, disappeared on the following day. Toward the end of January the pain reappeared accompanied by accelerated respiration. On examination the liver dulness was found to extend four fingers' breadth below the costal margin. There was also tenderness on pressure. Examination of the chest showed the presence of dulness and the absence of breath sounds below the angle of the scapula on the right side. Puncture in the seventh interspace yielded a greenish, purulent fluid containing typhoid bacilli in pure culture. A subsequent thoracotomy evacuated about two liters of pus. Operation did not afford relief and the patient died February 4. The autopsy showed cicatrization of Peyer's patches. The right lobe of the liver was almost entirely occupied by an abscess the size of the foetal head. The diaphragm was not perforated, although rupture into the pleural cavity was imminent. There was a purulent infection of the right pleura. Examination of the pus from the liver abscess showed the presence of bacilli identical with those found in the pleural fluid. In preparations from broth cultures the serum reaction was marked. All cultures were free from contaminating organisms. An examination of the pus for amœbæ was negative, and the author states that the patient had never had symptoms of dysentery.

CASE III.—Swain. A girl, aged five years, was first seen on December 8, 1897, toward the eighth week of a typhoid infection which had run a mild course followed by symptoms of relapse. For some weeks previously the temperature had shown marked fluctuations and on the above date a rigor occurred. A second

rigor occurred on December 11. About one week later the left lobe of the liver was palpable one inch below the ensiform cartilage and eversion of the left costal border was noted. There was tenderness on pressure. Rigors occurred on December 22, 23, 30, and January 1. The temperature on each occasion rose from normal or subnormal to 103° to 105° , being intermittent in type during the intervals. On the latter date the margin of the liver could be felt midway between the ensiform cartilage and the umbilicus. Fluctuation was absent. The upper limit of hepatic dulness in the axillary line remained at the normal level. Pain was complained of but tenderness was not now a marked feature. The general emaciation was extreme. January 3 (twelfth week) laparotomy was performed and about six ounces of bile-stained pus and fluid evacuated from an abscess cavity in the left hepatic lobe. The patient recovered.

Cultures made at the time of operation upon agar showed a few colonies of *Staphylococcus pyogenes aureus* and many colonies of short bacilli with rounded ends. The latter in broth produced cloudiness of the medium, were actively motile, and gave a characteristic agglutination reaction with typhoid serum.

CASE IV.—Perthes. A marine, aged twenty-two years, was admitted to the hospital, Pekin, December 3, 1900. The diagnosis of typhoid fever was confirmed later by the occurrence of the agglutination reaction. The infection is described as "moderately severe or light." Convalescence was established on the forty-second day and the patient was allowed up. On the forty-ninth day a single rise of temperature to 38.6° occurred. On the sixty-ninth day the temperature rose suddenly to 39.2° and the patient complained of severe epigastric pain. There was found a slight increase in the area of liver dulness, unassociated with jaundice. Enlargement of the liver was progressive. The temperature rose daily to 39° or higher. February 13, 1901 (eighty-first day), the upper limit of the liver dulness was at the fourth intercostal space in front and at the angle of the scapula behind, while the lower border was palpable four fingers' breadth below the costal arch in the right nipple line. There was slight tenderness on palpation in the epigastrium. The abdomen was otherwise flat and soft. Deep exploratory puncture in the seventh intercostal space in the anterior axillary line evacuated greenish-yellow pus. The liver was approached by the transpleural route, and a large abscess lying within the substance of the liver evacuated and drained. Streak cultures showed numerous bacilli and, in addition, streptococci. The former, isolated in pure culture, proved to be *Bacillus typhosus*. Agglutination occurred with typhoid serum.

Fever associated with diarrhoea persisted until May 9. It is not stated if an examination for amoebæ was made. The patient was discharged well on July 7.

CASE V.—Hühn and Joanovic. A forester, aged twenty-nine years, developed typhoid fever in January, 1901, the illness continuing until the middle of March. Toward the end of March there was a sudden rise of temperature associated with severe abdominal pain and jaundice. On examination there was found in the region of the gall-bladder a tumor, the size of a nut, painful on pressure. This swelling disappeared in a few hours, and a few days later the patient made a complete recovery and was allowed up. Toward the end of April a tumor the size of a child's head developed in the epigastrium, associated with jaundice and intermittent fever. On opening the abdomen there was found a multilocular echinococcus cyst of the liver filled with thin pus, from which typhoid bacilli giving the Widal reaction with typhoid serum were isolated. The patient recovered.

CASE VI.—Guinard. A male, aged forty-three years, developed typhoid fever, confirmed by Widal reaction, about the middle of October, 1902. Between October 28 and November 1 there were profuse intestinal hemorrhages. November 18, the patient developed abdominal and precordial pain with nausea and vomiting. November 21 the temperature reached 41° . The pulse rate was 150. There was severe thoracic pain. A temporary improvement followed. In the beginning of December the liver was noticeably enlarged. December 21 there was a sudden collapse, profuse sweating, and a fall of temperature to 36.4° . January 12 the lower margin of the liver reached to the iliac fossa. An exploratory puncture revealed the presence of pus. Tenderness over the liver was absent. There was no jaundice and tests for bile in the urine were negative. There had never been chills. Laparotomy was performed January 13. The abdomen contained abundant ascitic fluid. Puncture of the liver with the thermocautery evacuated an abscess containing about one and one-half liters of thick bile-stained pus. The patient died January 19.

Smears from the pus showed chains of Gram-positive cocci. Bacilli were not found. In twenty-four-hour bouillon cultures, however, there were, in addition to cocci, actively motile bacilli decolorizing with Gram's stain. These bacilli in pure broth cultures gave the characteristic agglutination reaction with controlled typhoid serum.

CASE VII.—Sennert. In the beginning of October, 1905, a painter, aged eighteen years, fell from a scaffold sustaining a severe injury to the right side. He was discharged from the hospital at the end of three weeks. Two months after the injury (early in December) he began to feel ill, and was admitted to the University Clinic at Halle, January 9, 1906, with a diagnosis of ambulatory typhoid. The patient later developed symptoms of subphrenic abscess. There was pronounced jaundice. January 26 an abscess in the dome of the liver was evacuated by the transpleural

route. The patient recovered. *Bacillus typhosus* was isolated in pure culture. Sennert concludes that at the time of the accident the patient sustained an injury to the liver with the formation of a hematoma which later became infected with the typhoid organism.

CASE VIII.—Venema and Grünberg. A female, aged thirty years, was admitted to hospital, June 18, 1906, at the end of the third week of typhoid fever. The diagnosis was confirmed by agglutination tests. July 15 two profuse intestinal hemorrhages were followed by collapse. At the same time the patient developed thrombosis of the right vena saphena parva. July 17 there was a sudden chill with a rise of temperature to 39.7° . The temperature reached normal July 22. After a fever-free interval of six days the temperature rose suddenly to 39° . July 31 enlargement of the liver was noted. There was spasm of the abdominal muscles in the upper zone. Symptoms were relieved by the application of ice; the temperature gradually fell to normal. From August 16 to 23 a second fever-free interval occurred. On August 24 there was a renewed rise of temperature. On examination there was found in the right hypochondrium a tumor larger than the fist, tense, elastic, and sensitive on pressure. October 5 an incision was made in the right hypochondrium and a perihepatic abscess evacuated, followed by incision and drainage of an abscess lying within the right lobe of the liver. Typhoid bacilli were grown in pure culture from the liver abscess, their identity, apart from cultural features, being conclusively demonstrated by controlled agglutination tests. The patient recovered.

CASE IX.—Lengemann. A girl, aged five and one-half years, developed typhoid fever (confirmed by Widal reaction) in September, 1906. October 14, about the fourth week, the temperature rose to 40.6° , falling again on October 16 to 37.2° . On October 19 it again rose to 40.3° with chill and complaints of pain in the right hypochondrium. The liver was found to be swollen and tender. A temperature of septic type continued until December 16 or 17, when a sudden fall to 35.2° occurred. December 21 puncture of the abdomen yielded pus from which *bacillus typhosus* was isolated. A laparotomy on December 22 disclosed a subacute peritonitis, presumably of five days' standing. There was marked injection of the serosa. An evacuated abscess cavity was found in the right lobe of the liver. From the peritoneal fluid typhoid bacilli were isolated in pure culture. Jaundice was absent throughout the illness. The patient recovered.

Group II.

Although bacteriological examination revealed the presence of typhoid bacilli in the pus from Cases XXV and XXVII, these cases have been included in the second series owing to uncertainty as to the location of the lesion.

CASE X.—Delaire. A woman, aged thirty-four years, after a post-typhoid fever-free interval of fourteen days, again became feverish and complained of pain in the region of the liver. Some days later the liver could be felt below the costal border; on the twentieth day it reached to the umbilicus with pronounced bulging of the epigastrium. There was tenderness on pressure. Fluctuation was not present. Abscess in the right lobe of the liver was diagnosed. Following sudden pain below the right breast, there appeared dulness in the right thorax extending halfway to the clavicle, with dyspnoea and spasmodic cough. Forty-eight hours later, during a suffocative attack, "streams" of very bitter green pus were coughed up. This act occurred several times with the simultaneous disappearance of the bulging described. All symptoms gradually disappeared and at the end of four months there was complete recovery. About one year later pain developed beneath the right costal border with chills and fever, as well as increasing enlargement of the liver. Bulging in the region of the liver was again noted. There was sensitiveness on pressure but no fluctuation. Later the whole of the right side of the abdomen became prominent, the dulness extending to the iliac fossa. The abscess apparently invaded the abdominal wall and burrowed downward. It finally ruptured externally near the anterior superior spine. Bile-stained pus was evacuated. The patient recovered.

CASE XI.—Chater. A female, aged twenty-six years, was admitted to hospital, May 28, 1873. In June, 1872, the patient had suffered from typhoid fever characterized by severe diarrhoea. Toward the termination of her illness she developed pain in the right side associated with chilly sensations and sweating. In September, 1872, the pain in the region of the liver became intense, radiating to the right shoulder and the right side of the neck as high as the angle of the mandible. Swelling in the hypochondrium was evident at the end of October, 1872. Diarrhoea alternated with periods of constipation. On admission there was an enormous swelling in the right side. Puncture on May 30, withdrew brownish blood-stained pus. Between this date and June 22 puncture was performed several times; about 281 ounces of pus were evacuated. June 21 there was a severe attack of abdominal pain referred chiefly to the right side, associated with nausea and prostration, and on June 22 there was evacuated by the bowel a large quantity of greenish-yellow material resembling that aspirated from the liver. The patient recovered.

CASE XII.—Sidlo. A girl, aged ten years, passed through a mild initial typhoid infection, the temperature reaching normal on the fifteenth day. On the seventeenth day the temperature again began to rise. On the thirtieth day it was normal. On the thirty-second day pain developed in the region of the liver and in

the chest. The liver was tender. There was a chill. On the thirty-fifth day the liver was first found to be enlarged. The skin and conjunctivæ were jaundiced. On the forty-third day the lower border of the liver reached the level of the umbilicus, and the right costal margin bulged greatly. Subcutaneous abscesses also developed in both mammary regions, in the right frontal region and in the right axilla. From the eightieth to the eighty-fifth day the axillary abscess, which was very large, rapidly decreased in size under observation; the other abscesses also subsided. On the eighty-fourth day an attack of severe abdominal pain with chill was followed by an evacuation from the bowel of blood-tinged purulent material. During the two following days there were numerous evacuations of a similar nature. The patient recovered.

CASE XIII.—Sorel. A foot-soldier, aged twenty-three years, was admitted to hospital July 16, 1882, with typhoid fever of a mild type. July 21 the patient complained of pain in the right hypochondrium and July 24 of pain on pressure in the epigastrium. The liver was not palpable. After July 28 (twentieth day) the fever became intermittent. August 18 subacute peritonitis was noted. The patient died on the forty-fifth day. At autopsy typhoid lesions in the ileum and colon were found. The right lobe of the liver showed on its convex surface a small, superficial hemorrhagic infarct which had not undergone softening. In the left lobe there was an abscess the size of a large orange. The liver was adherent to the diaphragm and posterior surface of the last part of the sternum and the origins of the right costal cartilages. These adhesions had rendered palpation impossible. The bile-ducts were healthy. There was also a subacute peritonitis about the level of the umbilicus, with a collection of seropurulent fluid in the right flank. This patient had never showed symptoms of dysentery.

CASE XIV.—Gerhard. A male, aged twenty-six years, was taken ill suddenly March 2, 1885, with vomiting and abdominal pain. Twelve days later the patient developed cough with impaired resonance and pleuritic rub at the right base. There was prominence of the right hypochondrium with tenderness on palpation; also tenderness in the epigastrium. The area of liver dullness was increased. April 4 fluctuation was noted over the right lobe of the liver. Owing to the general weakness of the patient an operation was not undertaken. Death occurred April 25. At autopsy there was found right-sided serofibrinous pleuritis. In the right lobe of the liver there was a large abscess as well as two small abscesses. The left lobe also contained a small abscess. The gall passages were normal. In the ileum there were found ulcerated as well as healed lymphoid patches.

CASE XV.—Gervais. A clerk was admitted to hospital March 15, 1886, with symptoms of typhoid fever. The disease ran a mild course and the patient left the hospital on April 18. There was

not, however, complete restoration of health. May 5 the patient was re-admitted, emaciated and weak. There was constant complaint of pain in the right side of the thorax. Examination showed dulness to be present over the whole of the right lung with the exception of the apex. There was displacement of the heart to the left. Death occurred May 25. At autopsy the liver was found to be greatly enlarged, containing in the posterior superior portion a large abscess communicating with the right pleural cavity.

CASE XVI.—Gervais. A convict, aged twenty-three years, was admitted to hospital September 25, 1885, with the characteristic symptoms of mild typhoid. During convalescence he was suddenly seized with severe abdominal pain associated with sweating, rapid pulse, elevation of temperature, nausea and meteorism. These symptoms were thought to be due to intestinal perforation. Three days later enlargement of the liver was noted with severe pain in the right hypochondrium. Still later fluctuation was made out in the right flank. Puncture yielded a grumous, bile-stained fluid having a fecal odor. The patient died November 9. At autopsy the whole of the right lobe of the liver was found to be occupied by an abscess which contained one liter and a half of pus of the same nature as that withdrawn. Peyer's patches showed traces of hypertrophy but no ulceration. In the large intestine were found cicatrices and traces of old ulcers. The spleen was enlarged. The patient had never had dysentery.

CASE XVII.—Gervais. An adult male was admitted to hospital June, 1886, with typhoid fever. In the fourth week of convalescence (July 28) the temperature rose to 39° and assumed a septic type. August 4 there was a tearing pain in the right side at the level of the ilium. The clinical note is headed: "Typhoid fever. Abscess of the liver opening into the intestine? Peritonitis following perforation?" The patient died September 10 "from abscess of the liver with peritonitis." When the abdomen was opened at autopsy, a large quantity of greenish purulent fluid escaped from the peritoneal cavity. The liver was merely a shell containing an enormous quantity of fetid pus, the color of wine dregs.

CASE XVIII.—Jahn. A dragoon was suddenly taken ill March 23, 1887, with typhoid fever. Convalescence was established April 6 (fifteenth day). April 19 the patient complained of marked weakness and severe pain on pressure in the epigastrium. Four days preceding these symptoms the temperature had risen to 40°, gradually subsiding under renewal of bath treatment. During the next three months the illness ran a chronic course. The temperature was at times remittent, at other times intermittent in type. There was gradual enlargement of the liver. Pain beneath the ensiform cartilage and along the right costal margin, chilly sensations, night sweats, and a sub-icteroid discoloration of the skin were also noted. Toward the end of this period there appeared tender-

ness on pressure beneath the lower ribs on the right side, with bulging of the chest wall, widening of the intercostal spaces and fluctuation. July 12 exploratory puncture in the ninth intercostal space yielded greenish-yellow pus. July 15 the liver was approached by the transpleural route and an abscess the size of an apple, extending into the substance of the liver, evacuated. A drainage tube was inserted. The patient recovered. No examination of the discharges was made for either bacteria or amœbæ.

CASE XIX.—Legrand. A soldier of marine infantry developed typhoid fever at Java in 1880, and during convalescence had symptoms of abscess of the liver. Puncture and lavage with solution of carbolic acid was carried out. The patient died. Autopsy showed a cicatrized abscess in the left lobe of the liver and a second abscess of large size beneath the convex surface of the same lobe.

CASE XX.—Legrand. A soldier of marine infantry at New Caledonia developed abscess of the liver during convalescence from typhoid fever in 1883. Puncture of the abscess with a large trocar was practised with only temporary relief. At autopsy there was found a large abscess in the dome of the right lobe of the liver with ulceration of Peyer's patches. The patient had not been exposed to dysentery.

CASE XXI.—Legrand. A discharged soldier developed abscess of the liver during convalescence from typhoid fever in 1885. Aspiration was practised. The patient died. At autopsy, in addition to the characteristic lesions of typhoid fever, there was found a large abscess in the right lobe of the liver as well as two small foci of suppuration in the left lobe.

CASE XXII.—Legrand. An artillery-man, who had not been exposed to dysentery, developed abscess of the liver during convalescence from typhoid fever in 1888. Autopsy revealed an enormous abscess of the liver with destruction of the whole organ.

CASE XXIII.—Legrand. An adult male developed abscess of the liver about one month after convalescence from typhoid fever. Puncture and lavage was carried out. The patient died. At autopsy there was found a solitary abscess in the right lobe of the liver.

CASE XXIV.—Legrand. An adult male, after a post-typhoid fever-free interval of about fourteen days, developed abscess of the liver. In spite of spontaneous rupture into the bowel the patient died. Autopsy revealed a large abscess involving the whole liver.

CASE XXV.—Maydl. A female, aged thirty-four years, came under observation with a diagnosis of right pyothorax one year after the termination of a typhoid infection of eight weeks. In addition to empyema Maydl determined the presence of a subdiaphragmatic abscess. The symptoms of onset were chills, fever, and epigastric pain radiating to the right shoulder. There was also œdema of the right thoracic wall. The full diagnosis was confirmed by laparotomy and a counter thoracic opening. Typhoid

bacilli and staphylococci (kind of staphylococci not mentioned) were recovered from the discharges. In this case the fever-free interval had been marked by alternating periods of diarrhoea and constipation, and occasional pain in the right hypochondrium. The patient recovered. There is no definite statement that the liver was involved.

CASE XXVI.—Ben Johnston. A male, aged twenty-eight years, had suffered from typhoid fever in the autumn of 1878. The illness was marked by intestinal hemorrhages. Convalescence was protracted. Attacks of diarrhoea were frequent. When seen in January, 1879, the patient complained of occasional nausea and vomiting, pain and acute tenderness in the right side, chills and sweating. The margin of the liver was palpable five inches below the costal border. Aspiration withdrew two pints of creamy pus. The cavity quickly refilled. Death occurred on the fourth day after aspiration. Autopsy showed the presence of a large abscess cavity in the right lobe of the liver. There was cicatrization of Peyer's patches.

CASE XXVII.—Caton and Thomas. A male, aged thirty-two years. Convalescence from typhoid fever was established on the twenty-fourth day and the patient allowed up on the forty-third day. The temperature rose at once and the patient was put back to bed for six days. He was again allowed up and had a chill and rise of temperature. No physical signs developed until two weeks later when there was found a dull area at the left base. Aspiration withdrew greenish-yellow pus. A transpleural operation exposed an abscess cavity in the liver five inches in diameter, with calcified walls one-eighth of an inch thick. The pus contained typhoid bacilli. At a second operation excision of the calcified wall was carried out. There were found adhesions to the spleen, stomach, transverse colon and omentum. The authors suggest that the condition was one of typhoid infection of a hydatid cyst of the liver. The possibility of a splenic origin cannot be excluded.

CASE XXVIII.—McCrae and Mitchell. A marine fireman was admitted to Johns Hopkins Hospital September 15, 1900, complaining of abdominal pain which had been present for one week; also cough, pain in the chest and shoulder when lying on the right side, and frequent vomiting. The bowels had been constipated until the day of admission, when numerous bloody stools were passed. Examination showed the presence of movable dulness in the right axilla and base: also tenderness and muscular resistance in the right hypochondrium. On September 19 jaundice was noticed. The Widal reaction was positive. The leukocytosis was 87,000. The patient was transferred for operation. When examined on the table, fulness in the right upper quadrant of the abdomen was noticed, as well as rigidity of the muscles and protective spasm on deep palpation. There was also a feeling as of a rigid mass beneath the muscles. Laparotomy exposed a large mass between the liver

and the abdominal wall. In separating the adhesions, 500 cubic centimeters of brownish fluid escaped, followed by thick yellowish pus with a slightly sweetish odor. On wiping out this cavity the upper surface of the liver was found to be excavated over an area of from eight to ten centimeters in diameter. Drainage tubes were inserted. The patient recovered. In preparations from the fluid and pus made at the time of operation no bacteria or amœbæ were found. Cultures were sterile.

CASE XXIX.—Wendel. An adult male had suffered from typhoid fever from September 30 to October 30, 1902. November 17, after a fever-free interval of eighteen days, pain developed in the region of the liver, increasing on coughing or deep breathing. On the following day the pain radiated to the right shoulder. The temperature was 38.9°. At the base of the right lung there was dulness with enfeebled breathing; also slight enlargement of the liver in a downward direction. Pressure elicited tenderness. November 23, an exploratory puncture in the eighth interspace, mid-axillary line, yielded pus. The eighth rib was then resected. Clear fluid escaped from the pleural cavity. Three centimeters within the liver substance an abscess was encountered and drained. No jaundice was noted throughout the illness, although bile pigment was present in the urine. Cultures taken at the time of the operation were sterile. The patient recovered.

CASE XXX.—Long. A male, aged nineteen years. On the nineteenth day of a mild typhoid infection (confirmed by Widal reaction) the patient complained of pain and tenderness over the lower margin of the liver. Three days later (May 30, 1903) the pain and tenderness were much more severe; there was bulging of the lower part of the chest and right kidney region. May 31 the leucocytosis was 19,000. Aspiration was followed by an incision parallel with the last rib. Two pints of purulent fluid with broken-down tissue were evacuated. The cavity extended upward into the liver. Cultures showed the presence of colon bacilli. The patient made an uninterrupted recovery.

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IRREGULARITY OF THE HEART AND AURICULAR FIBRILLATION.¹

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THE study of the pulse extends as far back as medical history, but it may be said without exaggeration that within the last fifteen years more progress has been made in certain directions than in the previous century. When the reason for this rapid elucidation of the subject is enquired into, it is found to be a simple one. Up to 1895, the human pulse only had been examined; since then the study has embraced the mammalian pulse; animal experiment has been called in to explain human abnormalities. Perhaps in no department of medicine has the employment of this new method of investigation—this *novum organum* of medicine—borne more immediate fruits. The whole of the new knowledge of the heart irregularities arose directly from experiments on animals. And I do not think I am doing injustice to the small band of investigators

¹ The inaugural Weir Mitchell Lecture of the College of Physicians of Philadelphia, delivered January 17, 1911.

of this subject when I say that many equally talented and original minds had previously studied the irregularities of the heart, and that the recent success is due not to any preëminent ability on their part, but to the means of investigation they employed and to the application of the knowledge acquired in the laboratory to the problems of the sickbed. Another point of interest in this connection is that none of these investigators, so far as I know, had in his mind the clinical problem when he commenced his work. As has so often been the case, casual observations pursued merely for the sake of knowledge, or as our critics say, "out of idle curiosity," have led to the elucidation of clinical problems of the greatest importance. It is well to put on definite record that Gaskell and Englemann took up the study of the frog's heart without knowledge of its bearing on the irregularity of the heart in man, that my work on the mammalian heart was undertaken to elucidate irregularities seen in the dog's heart under poisonous doses of digitalis, and therefore without bearing on therapeutics, and that Hering's subsequent experiments were inspired by similar "idle curiosity," in regard to certain irregularities observed on tying the aorta. I think it well to make these remarks as the memory of the medical profession is short. One uses the knowledge or the remedies with thankfulness and neglects to enquire how they were obtained.

The subject which I have selected to address you on tonight is one of the more recent additions to our knowledge of cardiac pathology. For many years a condition has been described in text-books of physiology as fibrillation, or vermicular or incoördinate movement, or sometimes as delirium; this delirium of the laboratory has been used in quite a different sense from the delirium cordis of the clinician, although curiously enough the clinical and physiological delirium prove to have an unsuspected relationship. This fibrillation is most readily induced by rapidly repeated electric shocks applied to the heart. When a rapid series of weak electric shocks is passed through a chamber of the heart, it responds with occasional extrasystoles, and if the strength of the shocks be increased an artificial rhythm may be elicited. As the strength of the current is further increased the rhythm accelerates, diastole becomes imperfect, and finally the chamber no longer reacts as a whole, but apparently individual fibres take up their own independent rhythm—fibrillation, incoördinate or vermicular contraction, or delirium. When this stage is reached, the chamber no longer expels its contents, and if the ventricle is the chamber involved, the circulation ceases and death results unless the normal rhythm returns. A number of poisons in large quantities have similar results—digitalis group, aconitine, barium, etc.—and it seems not unlikely that some cases of sudden death from "heart failure" are due to the ventricle passing into fibrillation. In dogs dying suddenly in the course of chloro-

form anesthesia, I have sometimes observed this fibrillation of the ventricle when the thorax was opened immediately.

When the auricle passes into fibrillation, the effects are not so serious, for the auricle is not essential to the circulation, and auricular fibrillation may last for hours in animals without serious consequences. When the electric stimulation of the auricle is of short duration, the chamber resumes its normal contraction immediately, but if the stimulation be continued for some time or if it be repeated, the fibrillation persists for some time after the electrodes have been removed, and after prolonged stimulation the phenomenon may continue for hours. Fibrillation of the auricle may be induced by the same poisons as that of the ventricle, and I have seen it occur in

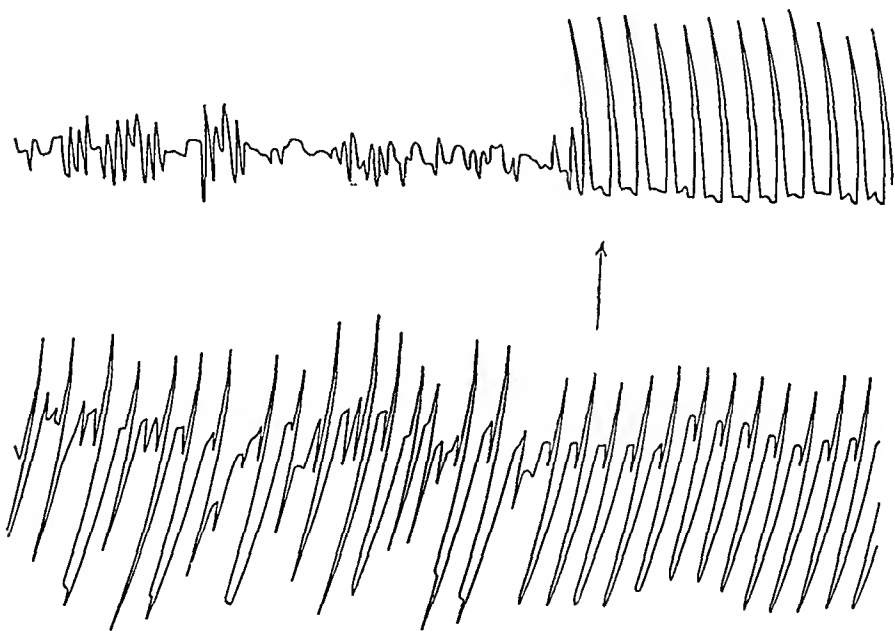


FIG. 1.—Tracing of the movements of the right ventricle (lower) and right auricle of the dog. To the right of the arrow, normal movements; to the left, auricular fibrillation from electrical stimulation of the auricle.

dogs from stimulation of the vagus. During fibrillation the auricle ceases to expel its blood and dilates widely. (Fig. 1.) The appearance of the chamber is very characteristic, but it is difficult to picture it unless it has been seen; instead of the short shock contraction which is characteristic of the normal auricular movement, one sees a quivering surface, each fiber of which seems to act independently of the others. A somewhat similar quivering is sometimes seen in the tongue and may be more familiar to you. Impulses continue to pass from the auricle to the ventricle as fast as they can be transmitted through the connecting band of His, but they are irregular, no two beats occurring at the same interval, and the strength of the contractions varying extremely. In particular there is no definite

relation between the strength of the contraction and the preceding pause. These irregularities are, of course, reflected in the radial pulse and in the apex tracing. In 1899, I suggested that the tracing of the arterial pulse in the dog (Fig. 2) during auricular fibrillation presented a striking similarity to the pulse known clinically as *delirium cordis*, and two years later I had the opportunity of examining a case of rapid irregular rhythm in a patient, which appeared suddenly, lasted for an hour or two, and then changed to the normal rhythm for some hours (paroxysmal tachycardia). The sphygmographic tracing presented such a marked similarity to that obtained from dogs during auricular fibrillation that I concluded that in this patient the cause of the irregularity was the same—auricular fibrillation.



FIG. 2.—Tracings from carotid of dog. The lower represents the normal pulse; the upper was taken during fibrillation of the auricle from rapid electrical stimulation. (Cushny and Edmunds.)

Unfortunately the method of taking the jugular pulse was unknown to me at the time (1901) and there was no way of confirming my diagnosis. When I and Edmunds published this view in 1906,² it was received with sympathy but incredulity by several writers on irregularity of the heart, the difficulty raised by them being that it was impossible to conceive of auricular fibrillation persisting for weeks or even years, while cases of tachycardia were known to have lived for this time. When I put my view to Mackenzie, he was struck by its applicability to a series of cases which he had described in which every trace of auricular activity had disappeared, and in which he had concluded that the auricle was entirely paralyzed. He agreed that my view would equally well explain these cases, in which he had found hypertrophy of the auricle at autopsy, which scarcely agreed with a paralysis of this organ; but the idea of auricular fibrillation was new and unknown to him as to most clinicians, and though some mention of it may be found in his papers about 1907, he had abandoned fibrillation for another explanation. Quite recently our view had been proved correct by the researches of Rothberger and Winterberg,³ and especially by those of Lewis.⁴ Auricular fibrillation is a common form of heart irregularity in man,

² Paroxysmal Irregularity of the Heart and Auricular Fibrillation, AMER. JOUR. MED. SCI., January, 1906.

³ Wien. klin. Woch., 1909, June 17, p. 839.

⁴ Heart, 1910, i, 306.

in fact, is much the most common cause of serious and prolonged irregularity.

It is therefore of importance to consider the characters of this irregularity as seen in man. And these may be stated shortly: (1) Very irregular pulse, the strength of successive beats bearing no relation to the preceding pause, and (2) disappearance of all trace of auricular activity in the jugular, liver, apex, and esophageal tracings, and in the electrocardiogram. In mitral stenosis the systole of the auricle is indicated by a murmur (presystolic), but when fibrillation is present this also disappears. This condition of auricular inactivity was detected and first described by Mackenzie, to whom we owe the recognition of this form of heart disease as a distinct pathological entity; as far as the clinical picture is concerned, his work has not received nor needed any amplification from other hands. It has been known by many names, such as *delirium cordis*, *nodal rhythm*, *ventricular form of the venous pulse*, *pulsus irregularis (perpetuus)*, but will, it is to be hoped, be known in the future by its essential feature, as *auricular fibrillation*.

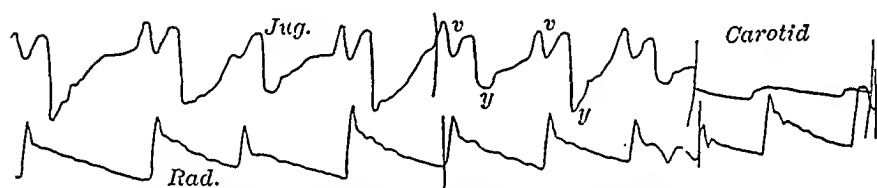


FIG. 3.—Radial pulse (lower) and jugular (upper) in a case of "ventricular form of venous pulse" (auricular fibrillation). (Mackenzie.)

The auricle ceases to expel its contents, and this is recorded in the jugular tracing by the absence of the *a* wave, and in long standing cases in which the auricle has lost its elasticity entirely, by the disappearance of the negative wave, which in the normal tracing marks the auricular diastole. The auricle remaining dilated throughout the cycle, the tracing of the vein must, in fact, be the same as if the jugular bulb was attached directly to the tricuspid valves. The tracing obtained from it, therefore, shows the negative wave when the blood flows onward into the ventricle, and as this chamber becomes filled, the tracing rises more or less slowly to be jerked up suddenly when the flow is arrested by the ventricular contraction, and to fall again when the way is opened again by the relaxation of the ventricle. In the normal pulse the same thing occurs, of course, the ventricular systole cutting off the inflow of blood into the ventricle. But here there is not stasis in the veins, for the blood flows into the auricle and the wave *v* is not very marked therefore. There may be superposed on the upper part of the curve several waves from the reflection of the carotid pulse and other causes, but

the essential feature is the absence of *a* and its following negative wave.

Wenckebach and Mackenzie have observed occasionally in the venous tracing a series of undulations during the pause of inactivity of the ventricle. It is not yet determined whether these arise from the feeble movements of the auricle, but it seems not unlikely that these may be transmitted through the swollen vein when they are of the coarse variety and the beat is slow. Lewis has observed them also in the dog.

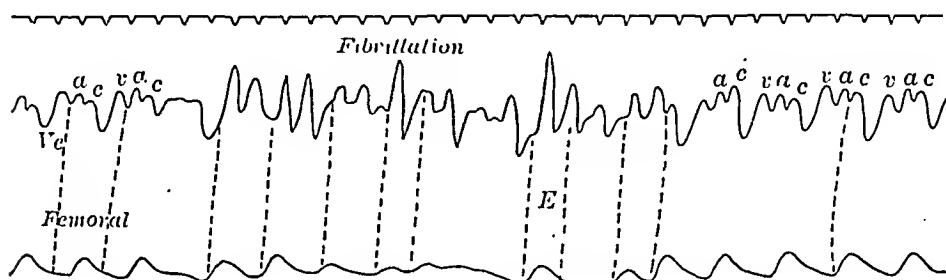


FIG. 4.—Jugular pulse (upper) and femoral (lower) in dog. To the left the heart is normal during three beats. Then auricular fibrillation is induced by electrical stimulation and again the normal rhythm returns in the last four beats. (Lewis.)

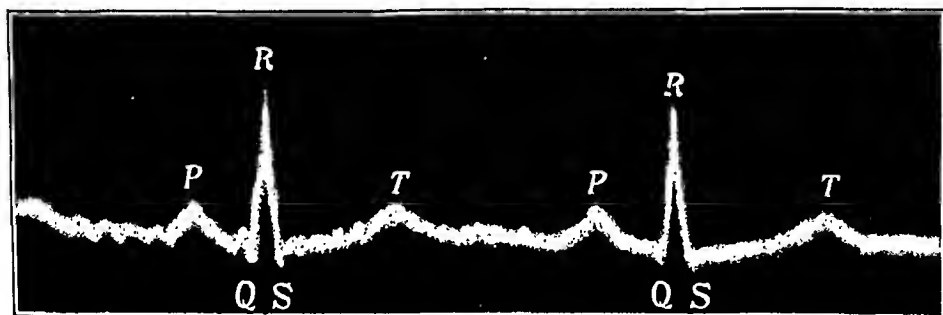


FIG. 5.—Normal electrocardiogram in human heart.

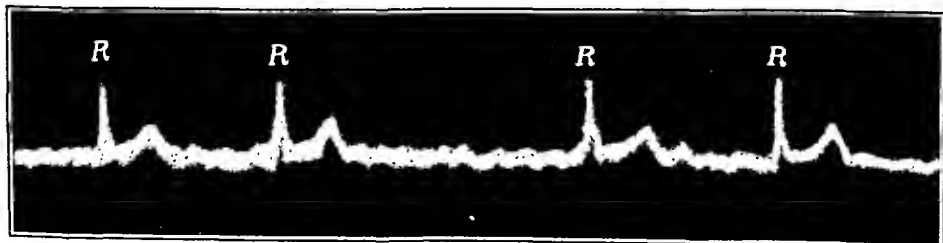


FIG. 6.—Electrocardiogram of dog during auricular fibrillation. (Lewis.)

It remains only to consider the changes seen in the electrocardiogram in this form of irregularity. When the electrical changes in the normal heart are recorded photographically by means of Einthoven's string galvanometer, each cycle is seen to cause a series of

waves which have been lettered *P*, *Q*, *R*, *S*, *T*. Of these *P* arises from the auricle, and is positive, and is followed by the small negative wave *Q*. Then *R*, a marked and sudden positive wave, followed by a depression, *S*, and a lower flat wave, *T*, all arise from the ventricular contraction. In auricular fibrillation in animals and in man, *P* disappears, the auricle not undergoing any active contraction. *R*, *S*, *T*, remain unaltered in essentials though, of course, the periods between each group vary in length, corresponding to the irregularity of the ventricular rhythm. The fact that *R*, *S*, *T* remain practically unaltered indicates that the ventricular contraction originates at the normal point and follows the normal course, and suggests that it is the response to an impulse descending from the auricle by the normal path through His' bundle. So far we have not progressed much further than with the jugular tracing which also shows the *a* to be absent. The convincing feature obtained by the electrocardiogram is the presence of a new series of undulations

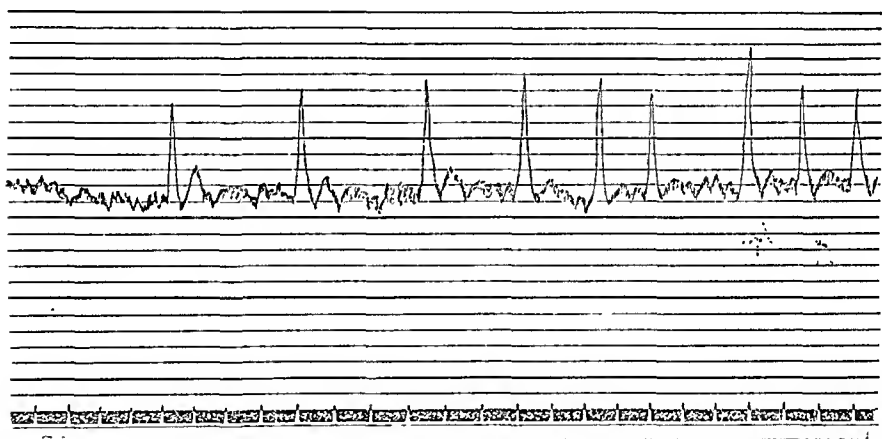


FIG. 7.—Electrocardiogram of patient during fibrillation of the auricle. (Rothberger and Winterberg.)

(450 to 900 per minute) on the curve, whether this is obtained from animals in fibrillation or from patients. These are seen throughout the electrocardiogram as far as they are not obscured by its other features and occur in no other known condition in either animals or man. They continue during the period of inactivity of the ventricle, and are more pronounced when the galvanometer is connected with the skin over the auricles than when the leads are taken from other parts of the heart. In fact, they may be little marked when the current is led off from the ventricles. And they are most marked of all when the fibrillating auricles of the dog are directly connected with the galvanometer. When the fibrillary contractions cease in experiments on the dog, these waves disappear, and in paroxysmal tachycardia in man they vanish also on the resumption of the normal

rhythm at the end of the paroxysm. I may be prejudiced in favor of a rather neglected offspring, but it seems to me that the observations of Rothberger and Winterberg and Lewis place auricular fibrillation upon an indisputable basis as occurring in man and as being the cause of the marked irregularity of the heart in question. But to those who are unfamiliar with the electrocardiograph, further and ocular proofs may be vouchsafed. It is true that no one has seen auricular fibrillation in a living man, though it occurs in the surviving human heart when it is perfused with Ringer's solution. But there is a disease in the horse marked by irregularity of the heart very similar to that met with in man and known as "tumultuous heart." This lasts for months and years in the horse, but renders it so weak and useless that as a general rule it is shot. In a horse destroyed in this way and immediately opened, Lewis found the auricle in fibrillation resembling that observed in dogs experimentally. The condition was of long standing, the proof is *ad oculos*, that the fibrillation is the cause.

During auricular fibrillation impulses are probably showered upon the auriculoventricular fibers in indefinite numbers, but these are capable of conveying only a certain proportion of them, and the rate of the ventricle is determined by the number it receives, that is, the number conducted by the bundle of His. As a general rule this is large, and the pulse is rapid (100 to 150). But in a certain proportion of cases the bundle is affected and can convey only a smaller proportion of impulses, and the pulse is then slow. The passage of the impulses is irregular and this accounts for the great irregularity of the ventricular beat and of the pulse. In one case Lewis⁵ observed auricular fibrillation with complete block of His' bundle, so that the ventricle had its own slow rhythm, which was quite regular, while no sign of auricular beat could be found in the venous tracing; the case, in fact, was a typical one of heart block as far as the ventricle was concerned, and differed from the ordinary type only in the auricle fibrillating; frequent attacks of unconsciousness were observed in this case as in ordinary heart block in which the Stokes-Adams syndrome is presented.

Fibrillation of the auricle thus playing an important part in cardiac disease in man, it is of interest to note any further points known regarding it in animals, in which it has long been recognized. It may be caused by stimulation of the auricle with rapid electrical shocks, or by the use of certain drugs which act on the heart muscle, such as digitalis or barium in large doses. It is also induced occasionally by stimulation of the vagus in dogs, and stimulation of this nerve seems to favor its development generally, for Winterberg⁶ found that weaker stimulation of the auricle caused fibrillation more readily during vagus stimulation than in other conditions. In a

⁵ Quart. Jour. of Med., 1910, iii, 273.

⁶ Pfüger's Archiv, cxvii, 223.

number of my earlier experiments on the heart I found the auricle in fibrillation and attributed this to reflex stimulation of the vagus. When fibrillation of the auricle has been developed, vagus stimulation in rare cases appears to arrest it, and in others renders the movement a finer one, but apart from this smaller movement it has no obvious result as far as the auricle is concerned. Vagus stimulation slows the ventricle, however, during auricular fibrillation, and renders the rhythm less irregular; this slowing of the ventricle arises from fewer impulses reaching it from the auricle from the passage through His' bundle being rendered more difficult through the inhibition. If the stimulation is strong in fact, complete heart block may be induced in some animals, and the ventricle then beats with a very slow and regular rhythm.

In man stimulation of the vagus by pressure on it in the neck has the same effect, the rate of the pulse slowing to a marked extent (Wenckebach)³, but the fibrillation continues and the rapid rhythm returns when the stimulation ceases. Removal of the vagus influence by giving atropine quickens the pulse but does not remove the irregularity except in very rare cases, its only effect being to facilitate the descent of impulses through His' bundle. The accelerator nerves seem to have little effect on the fibrillation, but may retard it to some extent (Winterberg).

The etiology of the condition in man is not yet determined, in fact its existence has been definitely proved only within the last year. In certain cases, as for example, that first described by Edmunds and myself, the attacks of fibrillation come on and relapse to ordinary rhythm so suddenly that one is disposed to regard them as due to some nervous influence, and since in animals vagus stimulation favors fibrillation and may induce it, I think it is justifiable to regard some of these cases as of nervous origin, as, indeed, we did in our first case. I am encouraged to this view because Hering found in one case that atropine, by removing the vagus action, restored the regular rhythm. Rothberger and Winterberg suggest that in early cases in which the fibrillation is not fully established the action of the vagus may be essential to its maintenance, and the removal of this favoring condition by atropine may be sufficient to restore the normal rhythm. When the fibrillation is fully developed, however, atropine does not arrest it. In other cases fibrillation occurs after the presence of more or less numerous auricular extrasystoles have been observed for some time previously; these extrasystoles indicate an abnormal irritability of the auricle muscle and the fibrillation is merely a further development of this condition. In animals, stimulation of the auricle with weak shocks causes extrasystoles and under stronger stimulation fibrillation is developed. In some cases both these factors, inhibition and abnormal irritability,

may contribute to the result. Thus in two cases which I have seen there was an extremely rapid regular pulse running to over 200 per minute, the rapidity being due apparently to extreme irritability of some point in the auricle which had taken up the rhythmogenic function. In both these cases digitalis slowed the pulse and at the same time induced short phases of fibrillation; I suggest that here the two factors of excessive irritability of the auricle and inhibition (from digitalis) were present and the fibrillation resulted. In a third case, in which the pulse was regular and rapid (90 to 100), digitalis in large doses induced sudden auricular fibrillation with a slow pulse (60 to 70), which after some hours as suddenly assumed its former rate and rhythm. Here I cannot help thinking that the arrhythmia was induced by the inhibitory action acting on a very excitable auricle, the excitability perhaps being due to the muscular action of digitalis.

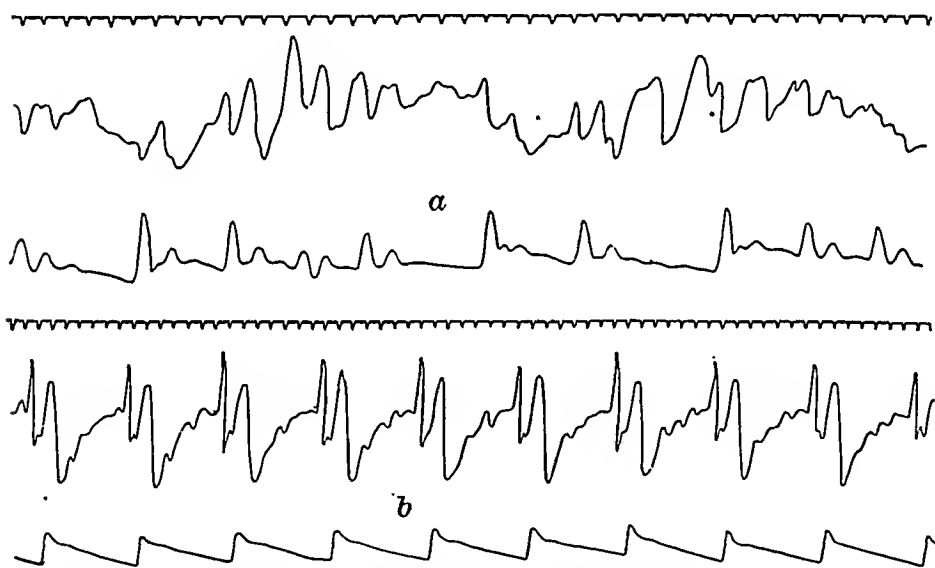


FIG. 8.—Radial and jugular tracings in patient during auricular fibrillation; (a) before treatment, (b) after treatment with digitalis.

Fibrillation may be suddenly developed and pass off again in a few minutes or a few hours or days; it is, in fact, present in many cases of paroxysmal tachycardia, though perhaps not in all. On the other hand, it may persist for many years, in some cases not interfering with ordinary avocations, but generally reducing the patient to a more or less invalid existence. In some cases sudden death has occurred probably from the fibrillation extending to the ventricle.

The diagnosis may be made with a fair amount of accuracy from the radial pulse alone. No condition is known in which the same degree of irregularity and the same variation in the strength of the contractions with respect to the interval preceding them are met with. On the other hand, in young persons, fibrillation may be present

without any striking irregularity of the pulse. But an absolutely certain diagnosis requires the use of the jugular tracing. When there is no *a* wave in this and the radial pulse has the characteristic irregularity the condition is certainly auricular fibrillation.

As regards the treatment of the condition, no disease of the heart responds so satisfactorily to digitalis and its allies as auricular fibrillation. In fact, were it not for its almost specific action in fibrillation it may be questioned whether this series would enjoy the reputation it has in heart disease. But not all cases of fibrillation react thus brilliantly to digitalis; the slow irregular heart in which fibrillation is accompanied by impaired conduction is comparatively little improved. The condition which responds to digitalis most readily and satisfactorily is the rapid irregular heart of old rheumatic disease, in which fibrillation is present along with good conductivity through the bundle of His and a readily responding ventricle. Here digitalis reduces the pulse rate rapidly from 120

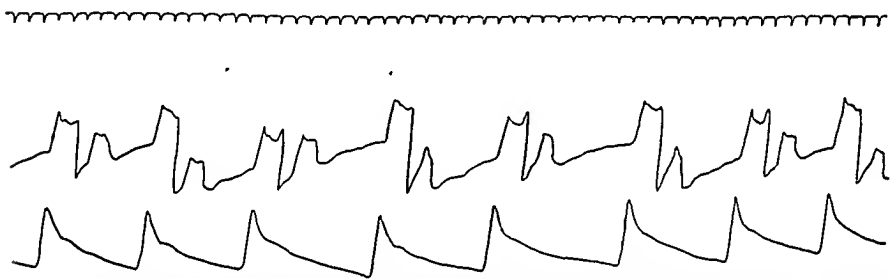


FIG. 9.—Radial (lower) and apex (upper) tracing in fibrillation treated with large doses of digitalis. Coupled beats (begemini) are seen in the apex tracing, but the extrasystoles are too weak to cause a pulse in the radial.

to 150 to 60 to 70, and as the pulse falls the whole of the symptoms improve. If the drug be pushed the pulse continues to fall and may reach 40 to 50. Beyond this digitalis generally induces other symptoms from the gastro-intestinal tract so that its dose has to be reduced. If it is abandoned altogether the previous condition soon returns, often in a less marked degree, and we have found it advisable to continue the treatment for many months. Digitalis does not arrest the fibrillation of the auricle, but it certainly reduces the number of impulses which reach the ventricle and thus lessens the rate of that chamber. I am not convinced that this reduction of rate, which is undoubtedly mainly inhibitory in nature, is the only effect of digitalis, though it is the only one which we can ascertain with certainty at present, and undoubtedly plays an important role in the action.

When digitalis is administered in auricular fibrillation and the pulse is slowed, the rhythm becomes more regular and the beats more equal in strength, though complete regularity is not attained unless complete block is induced. If the drug is pushed a curious

new form of irregularity often presents itself in coupled beats or continuous bigeminus in which each beat of the ventricle that arises in the normal way from an auricular impulse is followed by a contraction arising from the ventricle itself.

In connection with the treatment of fibrillation with digitalis, I may again remind you that an attack of this condition may in certain circumstances be precipitated by this drug.

In animal experiments various other measures have been found useful in arresting fibrillation, but these are all inapplicable in human patients. Thus I have found that cooling the heart with iced saline is often successful, while Gottlieb found that camphor perfused through the vessels seemed to have some effect in retarding its development. Hering recommends the perfusion of potassium chloride until the heart ceases all movement, and then restores it by means of Ringer's solution perfused through the coronaries. I merely mention these methods to show their inapplicability, so that no one may be induced to attempt the treatment of this condition by means of potassium salts.

PERFORATED ULCER OF THE STOMACH AND DUODENUM.

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WITHIN the past two years I have had four cases of perforating ulcer of the stomach or duodenum, several of which show points of marked interest in reference to the diagnosis, treatment, and end results. They are as follows:

CASE I.—Mr. Samuel M., referred by Drs. Ullom and Johnson, was admitted to the Germantown Hospital September 17, 1908. He gave a history of chronic dyspepsia, associated with vomiting and localized pain in epigastrium. He had been a sufferer from these symptoms for years. At 11 A.M. on the morning of admission he was seized with sudden, agonizing pain in the upper abdomen. The pain, which was extremely severe, radiated to the back and seemed to have its point of greatest intensity in the right iliac fossa. His abdomen was generally rigid, being most marked in the epigastric region. He was exquisitely tender over McBurney's point. There was no very great tenderness of the upper abdomen. He was operated on at 1 P.M., two hours after the onset of the attack. When the peritoneum was opened, gas and gastric contents escaped. The greatest quantity of fluid and debris was found in the right iliac fossa, although there were large quantities

throughout the peritoneal cavity. A hole large enough to thrust one's thumb through was discovered in the duodenum, one-half inch from the pylorus. This was closed by through-and-through sutures and oversewn with two layers of Lembert's suture. The drainage was placed through the wound to the site of the perforation and there was drainage through a button-hole incision above the pubes. For the first forty-eight hours after operation the patient had anuria, after which time the kidneys began to functionate. There was no evidence of either leakage or peritonitis. The material from the drains consisted of serum, with a small amount of stomach contents. Gastro-enterostomy was not done on this patient for the reason that the anesthetist reported the man as dead when the perforations had been closed. I believe, in view of the subsequent events, that had it been possible to have performed a gastro-enterostomy, the man might have recovered.

Seven days after the primary perforation the patient had a second perforation, with the same characteristic symptoms, resulting in death. The postmortem examination showed that there had been no leakage through the original perforation, and, while there was very little healing, the stitches had held it tight. The second perforation had occurred three-fourths of an inch from the first one, and when the duodenum was opened it was discovered that both perforations had occurred in the same ulcer, which was horseshoe-shaped, corresponding to the curve of the duodenum. There were four other ulcers of the duodenum. Dr. Ullom examined the specimen under microscope and discovered no malignant change.

CASE II.—Virgil H., aged forty years, was admitted to the German Hospital November 11, 1908; discharged January 16, 1909. The history was unfortunately overlooked and can be remembered only in outline. The family history is unimportant. For some years the patient had been troubled with indigestion, distress after eating, and pain in the epigastrium, with eructations of gas and occasionally nausea and vomiting. He had been treated palliatively and had tried sanatorium treatment at Battle Creek and the use of health foods without success. Ten days before admission the patient, while walking along the street, was seized with severe pain in the hypochondrium, radiating to the back and the right chest, accompanied with nausea and vomiting, and since then he has had chills, fever, and sweats. Bowels regular. Deep breathing gave him pain in the right hypochondrium. He gradually became greatly prostrated and weak. There was a tender localized mass in the region of the gall-bladder and a tentative diagnosis of empyema of the gall-bladder was made.

On November 12, under ether anesthesia, an incision was made through the upper right rectus. The pylorus and duodenum were found plastered tightly to the under surface of the liver, which was itself quite adherent to the abdominal wall. Upon gently releasing

these adhesions, a large subphrenic abscess was encountered lying beneath the right vault of the abdomen, and a considerable quantity of yellowish, foul-smelling pus was evacuated. There was some soiling of the general peritoneal cavity. On the anterior surface of the stomach, about three inches from the pylorus, a small perforation was found, which had been closed by the adhesions which bound the stomach to the edge of the liver. The edge of the perforated ulcer was turned in by chromic gut suture and oversewn by Lembert sutures of linen thread. The abscess cavity was drained by a rubber tube, emerging through the anterior wound, and a tube was also inserted through a counter puncture through the right loin. Three pieces of gauze were placed about the stomach, pylorus, and subhepatic surface. Fearing soiling of the lower abdomen, a glass tube was inserted in the pelvis through a suprapubic stab. The incision was partly closed by through-and-through sutures of silkworm gut.

The patient recovered without any unusual symptoms, and upon leaving the hospital had a small discharging sinus above the pubis.

Five months after the date of operation a piece of gauze one inch wide by five inches long was passed through the suprapubic sinus, which had persisted since the removal of the glass drainage tube. It was a piece of gauze of the tube dressing which had been cut thin at one place and had become separated and at the next dressing had been pushed through the tube and left there when the tube was withdrawn. Since this time all tubes at the German Hospital are dressed with selva gauze.

On the day of admission the leukocyte count was 25,280 and the hemoglobin 58 per cent. The urine showed a slight trace of albumin and casts for three weeks after the operation. A culture from the pus at the time of operation showed staphylococcus.

CASE III.—Andrew B., aged fifty-five years, was admitted to the Germantown Hospital January 16, 1909; discharged January 23, 1909. The family and early personal history is of no importance. For six months prior to admission the patient had been suffering from dyspepsia. Two years ago he had a serious and severe accident, sustaining fractures of the ribs, clavicle, and right leg. At half after four o'clock on January 15, 1909, while in a barber chair, the patient was seized by a sudden, sharp, severe pain in the upper right abdomen. He was able to walk to his home about one block away. Family remedies failing to give relief, he sent for Dr. Funk about 7.30 P.M. At this time his greatest pain and tenderness had localized in the right iliac fossa. On admission he had marked tenderness and rigidity in the right iliac fossa. Temperature, 100.2°; pulse, 100, and respiration 32.

He was operated on at once, an incision being made through the right rectus muscle, as we believed we had an appendiceal abscess to deal with. As soon as the peritoneum was incised, gas and pus

escaped from the cavity. A congested appendix containing blood-clots was removed. The incision was enlarged upward and plastic exudate was found under the liver and about the stomach. A perforated ulcer was found on the anterior surface of the lesser curvature of the stomach which was closed by chromic gut suture, and over-whipped by Lembert suture of silk. Cigarette and gauze drainage was inserted at the upper end of the incision and a glass drainage tube was inserted into the pelvic cavity. The wound was sutured between the drains. The patient apparently held his own until November 22, 1909, and then failed rapidly and died November 23, 1909, at 6.30 P.M.

Postmortem Examination. The ulcer in the stomach which had been sutured was found healed. A perforated ulcer was found in the duodenum about 2 cm. from the pylorus. There was considerable pus in the peritoneal cavity, and the intestines were matted together by plastic exudate. An indurated and suppurating area was found in the lower lobe of the right lung.

This case illustrates several important aspects of peptic ulcer: (1) The combined peptic ulcer of the stomach and duodenum; and (2) a primary perforation of a gastric ulcer and a subsequent perforation of a duodenal ulcer. Here again the value of a gastro-enterostomy presents itself. Temporary drainage by gastro-enterostomy might have prevented the second perforation.

CASE IV.—Joseph A., aged thirty-four years, born in Russia, was admitted to the German Hospital as a case of acute appendicitis with beginning peritonitis. The patient had felt well, aside from a poor appetite, until 2.30 P.M. on the day of admission. He had a piece of meat and tea for breakfast; nothing for dinner. At 2.30 P.M. he drank a glass of soda water and almost immediately was stricken with extremely severe pain across the right upper abdomen, which radiated into the right side of the back. There was some general abdominal pain but it was most intense in the upper abdomen. He was weak and perspiring profusely. He was doubled up like a jackknife, but obtained no relief. The bowels moved well in the middle of the forenoon. No definite gastric history could be obtained. Two weeks ago the patient began to belch up a little gas, and his appetite was poor. He complained of an occasional vague pain in the epigastric region. The only noteworthy thing about this pain was that on several different occasions it was relieved by vomiting. The patient never noticed blood in the vomitus or stool. No history of gall-bladder or appendiceal symptoms.

On admission, at 5.30 P.M., the patient had an anguished countenance, was restless, and complained of paroxysmal abdominal pain of severe character. Features were thin; his respiration was rapid and thoracic in type. Abdomen scaphoid, with board-like rigidity in the upper half; less marked but present in the lower half. Extreme tenderness above umbilicus, less marked below this point.

No more tenderness existed over appendix than in corresponding point on the left side. Liver dulness extended from the sixth rib to costal margin. The flanks were clear and soft, but a tender tympanitic swelling corresponding to the size and shape of the inguinal canal was found in that area on the right side. This felt like fluid under pressure and was easily reduced, but returned immediately on the release of pressure.

An operation was performed, with the diagnosis of perforated peptic ulcer. The patient took ether badly and in large quantities. On making an incision through the right rectus, some yellow, cloudy fluid was seen, and the bowel was slightly congested and distended. The appendix was examined and found negative, but it was removed in the usual fashion, but with some difficulty, on account of the high incision. The stomach examination was negative. The duodenum was examined and a large indurated ulcer was found in the anterior surface of the duodenum about 1 cm. from the pylorus. The ulcer was about 3 cm. in diameter. In the centre of it was a small pinhead perforation through which was escaping gas and fluid. A large gray area about 1.5 cm. in diameter, surrounding the perforation, was just about ready to slough out. The whole area was turned in with silk sutures, but this was difficult, on account of the poor quality of the tissue. A posterior gastro-enterostomy was done in the usual manner. A glass tube was inserted into the pelvis through a suprapubic incision and about 50 c.c. of cloudy yellow fluid was withdrawn. The tube was removed. The neighborhood of the perforation was mopped gently and the upper incision closed by tier sutures. The Fowler position and the Murphy treatment were employed after the operation. The further course was uneventful.

On admission the temperature was 99°, the pulse 84, and the respiration 26. A culture from the free abdominal fluid, made on November 22, was sterile. Examination of the appendix showed chronic interstitial appendicitis.

There is not any condition which the abdominal surgeon is called upon to treat in which prompt diagnosis, properly instituted treatment, and correct operative technique are more essential than in perforated ulcer of the stomach and duodenum. Ulcer of the stomach and of the duodenum can be considered together, not only because their pathology is practically identical, but also because, in view of the close relations of the two organs and their practically identical relations to other abdominal organs, the symptoms of perforation and the treatment thereof are practically the same.

THE FREQUENCY OF PERFORATION. The frequency of perforation of either gastric or duodenal ulcer is almost impossible to determine with any degree of accuracy. It has been estimated¹

¹ Pariser and Linder. Quoted by Deaver and Ashhurst.
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that 7 per cent. of gastric ulcers will perforate. It is very doubtful if this could be verified. Clinically, the number of perforations in a series of cases of gastric ulcer not previously treated surgically, will, I believe, be found to be considerably higher.

Upon duodenal ulcer there are practically no reliable statistics as to the frequency of perforation. It should also be borne in mind that up to the last few years many ulcers which were doubtless duodenal had been classed among "gastric ulcers of the pyloric region." Thus, some years ago duodenal ulcer as compared to ulcer of the stomach was considered rare; whereas now many operators, such as Mayo,² Moynihan,³ and Mayo Robson, whose experience in surgery of the upper abdomen is most extensive, now regard it as being more frequent than gastric ulcer. William Mayo has called attention to a possible explanation of this. In the Mütter Lecture before the College of Physicians of Philadelphia in 1908, he drew attention to the fact that the dividing line between the stomach proper and the duodenum is indicated by a sharply defined but not generally recognized line, recognizable superficially by the course of the pyloric veins. Previously the distinction between the duodenum and the stomach had been upon general lines, and in doubtful cases the diagnosis of gastric ulcer had been preferred to that of duodenal ulcer.

It must be stated, however, that in many series of perforated ulcers of the stomach and duodenum the number of perforated gastric ulcers is so far in excess of the ulcers of the duodenum that it seems doubtful whether duodenal ulcer is really so frequent as is stated by Mayo and Mayo Robson. Thus, in the experience of Miles,⁴ who published the largest series of perforated ulcers of the stomach and duodenum which have occurred in any one individual practice, of 46 perforated ulcers but 10 were duodenal, while 36 were gastric. In a series of 13 cases of perforated peptic ulcer operated upon at the German Hospital since 1904, 10 were duodenal and 3 gastric.

LOCATION OF THE PERFORATION. The location of the perforation, both in the stomach and duodenal ulcer, is almost invariably on the anterior surface of the organ affected. Perhaps this is because the anterior surface lacks the same support that is given by the underlying structures to the posterior walls. Thus, in statistics collected by Ashhurst and Deaver,⁵ 60.5 per cent. of duodenal ulcer perforations were upon the anterior wall, while the same was true of 71+ per cent. of gastric ulcers. By far the greatest number of duodenal ulcers were in the first part of the duodenum.

² Jour. Amer. Med. Assoc., 1908, p. 556.

³ Medical Press and Circular, London, 1908, n. s., lxxxvi, 110.

⁴ Edinburgh Med. Jour. 1908, n. s., xx, 106-117.

⁵ Surgery of the Upper Abdomen, 1909.

SYMPTOMS OF PERFORATION OF GASTRIC AND DUODENAL ULCERS.

The symptoms of the perforation of an ulcer of the stomach or duodenum vary. A perforation may be either acute or rapid, chronic or slow. Rapid perforations are particularly those in which the rupture of the viscus takes place into the free abdominal cavity so suddenly that no restraining barriers of adhesions have been previously formed. Such were Cases I, II, and IV of the series which I report.

The symptoms of a rapid gastric or duodenal perforation are very similar. The first indication of perforation may come at the time of the actual perforation, although in a certain number of instances premonitory signs, such as epigastric fulness and distress, make known the fact that there is some unusual disturbance of the diseased area.

Whether or not these premonitory signs are present, the first important symptom is a sudden sharp and agonizing pain referred to the epigastrium. The patient is invariably prostrated by the pain. Moynihan mentions several instances in which patients apparently succumbed to the shock caused by the extremely severe initial pain. The pain is, as a rule, well localized to the epigastrium, but may be referred, as in Case IV of the present series, where it was referred to the right dorsal region. After a comparatively short time the most acute pain leaves the patient, but he still has a marked feeling of pain, tenderness, and heaviness in the epigastrium. Vomiting in duodenal ulcers is so uncertain that it is not a symptom of the first importance. Hematemesis is rare in duodenal ulcers but comparatively common in gastric perforation. Elder, however, has reported a case of acute duodenal perforation in which the patient vomited bright red blood. This symptom is deceptive and hardly worthy of very great attention.

It was formerly stated that almost invariably there followed immediately with or after the pain a condition of shock. It is doubtless true that we find extreme prostration and weakness of the patient. The face is drawn and anxious, the patient perspires freely, and is somewhat pale or even slightly cyanosed in appearance. But as regards the pulse, temperature, and respiration, there is no evidence of shock until later, when a beginning septic peritonitis may give those symptoms. Thus, in Case IV, we find in an acute duodenal perforation, seen early, a temperature of 99° F., a pulse of 84, and respirations of 26 to the minute—certainly not significant of what is ordinarily considered as shock. The subjective symptoms, however, are not more important than those which we can discover upon thorough examination of the patient.

Abdominal palpation reveals an abdomen in which there is board-like rigidity of the recti, especially the right, and most marked in the upper abdomen. This extreme rigidity, which I have noted in my cases, is the most important diagnostic feature. The rigidity

accompanying perforated ulcer in the upper abdomen far exceeds that of anything but a most unusual appendicitis or gall-bladder lesion. In association with the rigidity we find early an abdomen which may be somewhat scaphoid, but as soon as the peritoneal reaction sets in distention begins. The abdominal muscles are held rigid to protect the underlying diseased area. The diaphragm is also in close relation to the infected field, therefore we find, as we would expect, that the patient's respirations are shallow and thoracic. This is due to nature's effort to put a muscular splint upon the whole peritoneal area surrounding the acute lesion. With the marked rigidity of the upper abdomen we note a general abdominal rigidity also—and one which gradually increases as the products of peritoneal infection spread over the whole abdomen.

Tenderness in the epigastrium in cases of perforation is to be marked early and is most severe. It has been stated that in duodenal perforation the tenderness is somewhat more to the right of the median line, while in perforations of the stomach it is to the right if the pyloric or prepyloric area be affected, and to the left if the lesion be in the body or either one of the curvatures of the viscus. The area of greatest tenderness, however, in either gastric or duodenal perforation may be about the umbilicus, and has even been referred to either iliac fossa, particularly, at times, to the right one. Leukocytosis is not always present immediately after the perforation, but appears as soon as peritonitis is in full activity. As it is an accompaniment of so many acute intra-abdominal inflammatory conditions, its usefulness is negligible and its only true value is as an indication of the patient's resistance. Moynihan and some others lay the very greatest stress upon anamnesis in the diagnosis of acute duodenal ulcer, and state that when a history of previous duodenal ulcer has not been obtained in those cases in which a perforated ulcer has been found, it is because the history has not been taken with sufficient care. In all my cases there was at least some history of gastric or digestive disturbance. Yet Elder,⁶ Watson and Korte,⁷ and many others mention instances in which the previous history does not point to ulcer of any sort. Korte, in a report of 18 gastric perforated ulcers and 1 duodenal perforated ulcer, says that of the 19 cases, 2 gave a history of very slight previous trouble, while 4 gave absolutely no history of disease in the upper digestive tract. We must make our diagnosis in acute perforation, then, largely upon the history of the immediate condition which causes the patient to seek treatment.

Case III of my series represents the class of subacute or slow perforations. These, as may be expected, are more common posteriorly where the adjacent viscera furnish support to the stomach

⁶ *Annals of Surgery*, 1906, xliii, 390.

⁷ *Archiv f. Chirurgie*, vol. lxxxi; *Berl. klin. Wchnschr.*, 1907, xliv, 226.

and duodenum, and act as limiting structures to prevent the spread of infectious materials. In Case III, however, the ulcer was anterior. When a gastric or duodenal ulcer perforates subacutely, the symptoms are, as a rule, more protracted and less severe than in acute perforation. The course of the lesion subsequently is entirely different, for instead of the onset as a general or diffuse peritonitis, we have the formation of a localized abscess, sometimes anterior but usually subphrenic. The latter term as used generally will include also abscesses which have no real nearness to the diaphragm but are merely intraperitoneal abscesses of the upper abdomen. Mayo Robson states that perforated gastric ulcer is the most frequent cause of subphrenic abscess—a statement that Deaver does not agree with, as in his experience appendicitis is the most common cause.

In addition to the general signs of perforation in such instances, we would have the local signs of a circumscribed collection, particularly if this be anterior. The whole course of the illness is less acute, and since the patient does not develop an acute and rapidly spreading peritonitis, we have the clinical picture of localized abscess, with systemic infection of the septic type. Chills, irregular fever, sweats, leukocytosis, etc.

DIFFERENTIAL DIAGNOSIS. The differential diagnosis of perforated gastric and duodenal ulcer is, as a rule, not difficult. There are, however, certain conditions which must be eliminated. Biliary colic may give pain almost as severe, and even temporary prostration as marked as that of perforated ulcer, but the subsequent hour or two with the failure of the case to show evidence of upper abdominal peritonitis will surely clear the diagnosis. Rupture of the gall-bladder is rare in the absence of definite history of previous enlargement and inflammation of the viscus. It is also absolutely far more rare than rupture of gastric or duodenal ulcer. Should it, however, occur in any instance in which the previous history did not point to a gall-bladder condition, I hardly see how it could be absolutely differentiated. In either case operation is indicated, so that the distinction is of no great importance. The conclusion that the primary pain of perforating ulcer cannot always be distinguished from that caused by disease of the biliary organs has been voiced also by Van Swerigen.⁸

The ileus may be considered to be the point of origin of the sudden severe pain. It should not, I believe, be difficult to differentiate even the most suddenly beginning intestinal obstruction from perforating ulcer. But it is interesting to note in this connection that in a series of 11 cases reported by Van Khantz,⁹ 2 were supposed to have had their symptoms caused by obstructions at the site of an

⁸ Jour. Amer. Med. Assoc., Chicago, 1908, li, 405.

⁹ Archiv f. klin. Chir., 1908, lxxxv, 700-717.

old hernia. Probably poor history taking and rapid and superficial examination account for this error.

Menstruation is mentioned by Moynihan as having three times in his experience given symptoms which led to the diagnosis of perforated gastric ulcer. This, however, is a most unusual error in diagnosis. Perforation of malignant growth of the large and small intestines cannot, of course, be accurately diagnosed or distinguished from other abdominal perforations unless previous history and examination point definitely to their existence.

Perforated jejunal peptic ulcer is identical in pathology and anatomy, and therefore also in symptomatology and treatment, to perforated gastric and duodenal ulcer.

Acute appendicitis is the diagnosis most frequently made where, in cases of perforated gastric and duodenal ulcer, a correct diagnosis has not been made. One of the four cases of my series was so diagnosed before being sent into the hospital. That this is not unusual will be seen by the appended table:

Operator or reporter.	Cases of perforated ulcer.	Diagnosis of appendicitis.
Von Khnatz	11	3
Peck ¹⁰	7	3
Federmann ¹¹	16 (op. 11)	2
Korte	19	2

The reason for this is twofold: (1) Acute appendicitis is the most common cause of intraperitoneal acute inflammation; and (2) perforated gastric and duodenal ulcer when discharging fluid or causing peritoneal infected fluid to form is, as a rule, so located that the fluids will gravitate toward the right iliac fossa.

Maynard Smith,¹² in a series of experiments carried out upon the cadaver, found that the fluid from such a source in a patient in a recumbent position followed the following course: (1) Downward in the direction of the right kidney pouch; thence (2) along the outer side of the ascending colon as far as the brim of the pelvis; thence (3) overflowed into the pelvis. Hence we can see why trouble of the appendix is so closely simulated, especially as Van Sweringen points out, after the lapse of about twelve hours.

It must not be forgotten that perforated duodenal ulcer and acute perforative appendicitis may be coincident. Indeed, Graham¹³ reports a case in which a perforated retrocolic appendix formed part of the wall of an abscess originating from a perforated duodenal ulcer.

Acute pancreatitis has been mistaken for a perforated gastric or duodenal ulcer. There is no doubt that the early distinction is

¹⁰ Med. Record, N. Y., 1907, lxxii, 930-934.

¹¹ Deutsche Zeitschr. f. Chir., 1907, lxxxvii, 443-481.

¹² Lancet, 1906, i, 895.

¹³ Annals of Surgery, 1904, xl, 447.

most difficult; but, as the case progresses, there is noted the gradual toxemia of pancreatitis, the absence of the characteristic rigidity of perforation, and the evidence of an infection of the omental bursa, and the marked symptoms of high intestinal obstruction—diaphragmatic pleurisy, diaphragmatic hernia.

Richardson¹⁴ in a most careful article has drawn attention to the frequency with which acute intrathoracic disease simulates the symptoms of acute intra-abdominal lesions.

Barnard¹⁵ reports an instance in which double basal pneumonia with a right diaphragmatic pleurisy in a patient with an unperforated gastric ulcer gave rise to symptoms leading to a diagnosis of perforation.

The appendix as a cause of disease simulating upper abdominal disease has come more and more into prominence within the last few years. I have already mentioned the frequency with which acute upper abdominal disease is diagnosticated appendicitis. While the reverse condition is not so common it must not be forgotten that appendicitis especially of the chronic variety often gives rise to crisis of pain referred to the upper abdomen occasionally accompanied by hemoptysis (Fenwick).¹⁶ The occurrence of pylorospasm as a result of chronic appendicitis is not common but nevertheless is mentioned by several authors, amongst them Deaver and Ashhurst. It might even be possible that an acute fulminating attack of appendicitis might give rise to the symptoms of perforated gastric or duodenal ulcer, but we are far more likely to find it a confusing element in the anamnesis when attempting to elicit a history of upper abdominal disease prior to the suspected perforation.

Finally the possibility of a diaphragmatic hernia must be considered, although this condition is practically never diagnosed during life except by operation.

Hysteria or unperforated ulcer with peritonitis may all give rise to symptoms very closely simulating those of perforated ulcer.

The distinction between gastric and duodenal perforation is not always difficult; in fact, Moynihan considers it comparatively easy in most instances. Sometimes the anamnesis makes the case clear at once. At other times the distinction is more doubtful, because the history is less clear. In either case the practical importance of the matter is not very great because our treatment is the same for both gastric and duodenal ulcer.

TREATMENT. The treatment of perforated gastric and duodenal ulcer is in its main aspects entirely surgical. Nothing is surer than the fatal termination of a perforative peritonitis of the upper abdomen in all but the rarest instances when a surgeon is not put in charge of the case. The patient's only chance for recovery under

¹⁴ Boston Med. and Surg. Jour., 1902, i, 399.

¹⁵ Lancet, 1902, ii, 280.

¹⁶ Dyspepsia, London, 1910, p. 78.

medical treatment is in the formation of a localized abscess with spontaneous evacuation other than into the general peritoneal cavity, a termination so rare that it need not be considered.

The time of election in operation for perforated gastric and duodenal ulcer is at once when the case is seen. All statistics agree that in those instances where acute perforation takes place and the infection is not circumscribed, early operations are by far the most successful. Thus, Van Khnatz had:

	Mortality, per cent.
5 cases operated in the first twelve hours; 3 died	60
1 case operated in the first eighteen hours; 0 died	0
5 cases operated after the first two days; 5 died	100

Or,

In the first twenty-four hours, 6 operated; 3 died	50
After forty-eight hours 5 operated; 5 died	100

Martens¹⁷ had in 11 cases 6 recoveries, all operated upon from two and one-half to twenty-six hours after perforation.

Robson and Moynihan¹⁸ give the following mortality in per cent. for perforated gastric ulcer: Under twelve hours, 28.5 per cent.; twelve to twenty-four hours, 63.6 per cent.; twenty-four to thirty-six hours, 87.5 per cent.; thirty-six to forty-eight hours, 100 per cent.; over forty-eight hours, 51.5 per cent had evidently had time to localize.

Patterson¹⁹ in a consecutive series found in cases operated under twelve hours, 47 per cent. mortality; twenty-four hours, 50 per cent. mortality; twenty-four to forty-eight hours, 83 per cent. mortality.

There are a number of reasons why it is of the utmost importance to operate early in cases of gastric and duodenal ulcer. In the first place, it is well known that in any peritonitis beginning in the upper abdomen early operation offers the patient the very best chance of recovery. Early operation avoids the absorption of toxins and anticipates the loss of the patient's vitality caused thereby. It enables us to intervene when the disease process is still localized to some extent and has not reached the stage of general peritonitis. In cases of gastric and duodenal perforation it is even more important, however, to deal with the resultant peritonitis early than it is in inflammations of the lower abdominal or pelvic viscera. I have mentioned the path of diffusion of the toxic fluids formed or liberated within the upper right quadrant of the abdomen. There is in so many instances no attempt at localization that often we have a rapid spread of infectious material in a purely mechanical way. Naturally, if we operate in the first stage of a perforation, this mechanical diffusion will not be far advanced and we have to deal with a more or less localized peritonitis instead of one which is diffused or general.

¹⁷ Deutsche med. Wehnschr., 1907, xxxiii, 1851.

¹⁸ Diseases of the Stomach, 1907, p. 101.

¹⁹ Lancet, 1906, i, 575.

Moreover, it has been pointed out by Murphy²⁰ and others that the diaphragmatic zone of the peritoneum is by far the most absorptive area of the whole membrane. Infectious materials are absorbed with far greater rapidity by the diaphragmatic peritoneum than by any other portion, and not only is this true but we have found that the whole upper abdominal peritoneum shares to a certain extent this great power of absorption. Thus, while a pelvic or lower abdominal condition, such as appendicitis or salpingo-oöphoritis, occurs in the area in which there is a certain possibility of defense against toxins, exactly the reverse is true of a perforated gastric or duodenal ulcer. On this account, again, it is most important to remove both the source of infection and the infectious material already formed at the earliest possible moment. I have no doubt that when it becomes the usual thing among medical men and surgeons accurately to diagnose such conditions early and to operate at once under practically all conditions, the mortality will be reduced to a point far below that reached by any operator so far.

The operation itself must accomplish three things primarily: (1) It must include some form of closure of the ruptured ulcer; (2) it must adequately provide for the drainage, etc., necessary for the care of the peritoneal condition; and (3) under favorable circumstances, it may seek to prevent a recurrence of the perforative process. It is, of course, imperative that at the time of operation we should locate the perforation itself. After making the incision into the upper abdomen, a foul fluid, possibly containing portions of foodstuffs, may be discovered. If this be caused by a perforated ulcer of the alimentary tract, we often have also an escape of gas from the wound. Our diagnosis is then certain. Before proceeding any further we should at least attempt to prevent further diffusion of infectious materials during the operation itself by the proper use of large gauze pads to wall off the infected area. I am certain that the proper use of such barriers to infection in all operations for localized or even diffused peritoneal infections is of the utmost importance. It should be our object to introduce at once these pads, not only so that they effectually limit the spread of pus, etc., during the operation, but also that by their rough introduction and handling they do not denude the peritoneum of its endothelial coat and thus give rise to the subsequent formations of adhesions. If the rough handling of the clean peritoneum may give rise to the postoperative adhesions, these are certainly more apt to form when infection is already present. These pads also act as a sponge while in the general peritoneum.

When the operative area has thus been limited we may proceed in our endeavor to find and close the perforation. In cases beyond the first few hours there is often quite an amount of plastic lymph

²⁰ Surg., Gynec., and Obstet., Chicago, 1908, vi, 575-598.

about the infected area. This should be removed only when it is in the road of the operator; otherwise it should not be disturbed, as there is reason to believe that it has a protective function. The omentum also has often come to the rescue and its adhesions should be gently separated so that we do not cause additional damage to the upper abdominal structures. Often, too, the omentum itself has covered the perforation and has acted as a temporary plug, preventing further escape of infectious material and localizing the peritonitis. By care in the use of our pads and careful though not slow operative procedures, it is often possible to complete the operation without further spreading the pus present.

When the perforation has been found there are several points which must engage the surgeon's particular attention. In the first place, it is always wise to determine whether or not the perforation is single. It is true that multiple simultaneous perforation of the stomach or duodenum is the exception rather than the rule, yet they have been reported. Secondly, we should endeavor to make sure that the ulcer is not accompanied by others not yet perforated but about to do so. In two of my cases, both of them ending fatally, and the only ones so ending, death was caused by the perforation of a second ulcer. In Case II of perforated duodenal ulcer, a second perforation was found in the same viscus, while in Case III, in which the primary condition had been a perforated ulcer of the stomach, death resulted from the subsequent perforation of a duodenal ulcer. Ulcers evidently about to perforate should be treated as if they had already done so.

When we have found the seat of perforation, several methods of closure are open to us. It is my usual course to invaginate the ulcer as far as it is possible without occluding the lumen of the bowel and then to sew all layers with a continuous catgut suture, repeated if it is thought necessary to strengthen it. To make the closure tight, it is then completed by a continuous Lembert suture of fine linen thread. I do not believe it is essential to cut away the edges of the ulcer. If invagination is complete the sloughing edges will separate into the lumen of the bowel when healing takes place.

Eve²¹ has lately suggested that the ulcerated area be excised by a longitudinal diamond-shaped incision, such as is used in pyloroplasty, and that the wound be then closed in the vertical direction, thus effectually avoiding narrowing the gut. In cases where such a narrowing seems especially likely, this method might be of use, but I have not as yet found it necessary.

When we have dealt with what appears to be the only perforation present we should investigate the viscus carefully to see if there is not another perforation. Gastric ulcers are multiple in about 8 per cent. of all cases; duodenal ulcers less frequently so; and per-

forations may also be multiple. Even when an ulcer has not yet perforated, it may be on the verge of doing so, and in that case we should deal with it exactly as if the perforation had already taken place. It must be remembered also that gastric and duodenal ulcers may exist coincidentally, as in Case III, reported previously.

Adequate drainage is of the utmost importance. When the ulcers have been closed, provided that gastro-enterostomy has not been done, the peritoneal cavity may be cleaned in the immediate neighborhood of the field of operation by mild swabbing with gauze pads. I do not believe that irrigation of the whole peritoneal cavity is ever necessary or even advisable. At its best it cannot fail to disseminate infectious material, though not necessarily spreading infection. With proper drainage and modern postoperative methods, we are far safer in allowing the peritoneum to take care of itself. Irrigation may do good—it has often done harm—and the chances for the latter overbalance the possibilities of its beneficial action.

We are often best able to insert our permanent or postoperative drain before the gauze packs have been removed. Our drainage should do two things: Drain the original site of infection. This is best done by a rubber tube containing gauze, with plain gauze about, if necessary placed through, the incision itself. This may be replaced by a stab wound to one side of the incision, allowing the latter to be closed in its entirety and thus, perhaps, making the abdominal wall stronger. The choice must rest upon the judgment of the surgeon.

Körte²² states that he considers a drain, as a rule, unnecessary but uses a pelvic drain where any drainage is indicated. I believe that we are usually safer in draining at the original site of infection. As the fluids of the upper abdomen always gravitate toward the pelvis, and particularly when we aid them in doing so by raising the patient in the bed, we should never force the pelvic peritoneum to deal unaided with the infectious material covering it. In all cases of severe, upper abdominal infection which might spread I employ a glass tube drain placed into the pelvis through a suprapubic stab wound and leave it in for two or three days until all danger of general peritonitis is past.

The question of gastro-enterostomy is one of great importance and is being largely discussed by surgeons today. Deaver and others claim that the drainage thus provided, be it temporary or permanent, will permit healing of the ulcer which may exist and thus prevent the liability to secondary perforation. Mayo and Moynihan do not advocate the procedure unless the lumen of the pylorus or duodenum is seriously diminished, as they claim that in the presence of a normally patulous duodenum or pylorus the artificial gastro-enteric opening will not functionate, and thus the object

²² Loc. cit.

sought for will not be accomplished; and, as the operation takes time and must be done on a patient who is already hard hit, it to this extent lessens the patient's chance of recovery. This problem is like so many more in surgery in that it can and should be used in certain cases and is strongly contraindicated in others, and its successful use depends on the judgment of the surgeon.

The after-treatment of perforated ulcer consists in rest for the part involved by the avoidance of food ingestion and peristalsis and by the use of appropriate measures of defence for the peritoneum.

The patient occupies the high Fowler position so that the infectious fluid may gravitate from the absorptive diaphragmatic area to the safer pelvic zone. No fluid is given by mouth for thirty-six hours and the patient is kept thereafter on a liquid diet and semi-fluid for eighteen days. The Murphy method of giving saline by continuous enteroclysis is employed routinely; otherwise the treatment is that of any section case for a grave lesion. Vomiting, and even nausea, if at all persistent, should be treated by lavage and repeated as often as it is necessary permanently to relieve vomiting.

THE CELLULAR ELEMENTS OF THE BLOOD IN TUBERCULOSIS.

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RED CELLS. The various authorities upon this subject seem to agree in that there is but little change, if any, from the normal in the red count or hemoglobin percentage in tuberculosis, excepting in advanced cases shortly before death when both are decreased, sometimes to a marked degree.

In the routine examination of the blood of cases admitted to Las Animas Hospital, we found this to be so uniformly true that we discontinued making the red count and the estimation of hemoglobin as routine procedures. In a large number of cases the reds averaged above 5,000,000 per cubic centimeter and the hemoglobin 85 per cent.

It has been found, however, that the red cells are pathological to the extent of resisting the hemolytic action of salt solution at least, and from this fact a method¹ of obtaining the hemolytic index

¹ The method for determining the hemolytic index is, briefly, as follows: Dilute the blood in the red cell pipette with an accurate 0.35 per cent. NaCl solution. Allow to stand five or ten minutes, and proceed to count the visible (non-hemolysed) red cells. Usually it will be possible, and preferable, to count the cells on that part of the slide used for counting leukocytes. In far advanced cases the central ruled area may have to be used. 150,000 divided by the number of cells found per cubic millimeter of undiluted blood will give the hemolytic index.

has been devised which is simple, rapid, and accurate. We believe the hemolytic index will prove of great value in differential diagnosis, but its greatest field of usefulness is in prognosis.

The lower the hemolytic index the less favorable the prognosis, irrespective of the stage of the disease as determined by physical diagnostic methods, clinical symptoms, etc., though, as a rule, a low hemolytic index will be accompanied by the physical signs and symptoms of advanced tuberculous involvement, and invariably by a low lymphocyte percentage. The normal hemolytic index is 1; cases in which it does not fall below 0.5 we regard as favorable, those not below 0.3 as guardedly favorable, those below 0.3 as unfavorable; in the majority of these latter cases death will occur in from one to ten weeks.

PLATELETS. In tuberculosis these present a normal or a reduced count, which is readily explained by the increased resistance of the red cells. It was while trying to determine the pathological cause of this resistance that lead one of the writers² of this paper to discover that the normal red-blood cell is nucleated, these nuclei becoming the platelets upon the destruction and disintegration of the red cells.

WHITE CELLS. The following data relative to the total white and differential counts has been obtained from 577 cases, in which the blood has been studied in intimate association with the clinical side of the cases.

We regret that our results are somewhat incomplete, owing to the fact that we have not had incipient cases under treatment. The cases being divided as follows: 133 moderately advanced cases, in which the local involvement was confined to the lungs, both lungs presenting lesions in each case; 412 advanced cases, in all of which both lungs were involved, a number of these cases presenting secondary involvements of joints, bone, throat, and the genito-urinary tract; 32 far-advanced cases, most of which presented terminal involvements of larynx, intestinal tract, liver, kidneys, spleen, and brain. Had incipient cases entered into these statistics, it seems probable that the only difference made in the table would have been a reduction of the average white count.

WHITE COUNT. The text-books furnish us with but little information of value relative to the white count, simply stating that in tuberculosis it is slightly increased, averaging about 13,000. This is true, but very misleading. In reality the white count steadily increases as the disease progresses, and, per contra, decreases as the disease improves. The various stages of the disease can be determined with marked accuracy by the white count in most instances, thereby checking the physical and clinical findings. This is well shown in the table given below.

² King will contribute an article on the Erythrocytic Nuclei of Normal Human Blood to the Journal of Medical Research, vol. xxiv, No. 1.

Polymorphonuclear Neutrophiles. The teaching has been that the percentage of these cells is reduced in tuberculosis, but by referring to the table it will be seen that the reverse is the case. Contrary to the general opinion, we do not believe that these cells have any pronounced phagocytic action in tuberculosis. On the contrary, an increase in the percentage of these cells makes the prognosis less favorable.

Lymphocytes. We have also been taught that in tuberculosis the lymphocytes are increased; in fact, that an increase in these cells is diagnostic of the disease. That neither of these premises is correct is well shown by the table. They are not even an index of the stage of the disease, which is also well demonstrated in the table by the figures under the heading lymphocyte percentage range.

We believe them to be the most important white cell in relation to tuberculosis, considering them to be the phagocytic agents in this disease for the following reasons:

1. Because patients admitted with a high lymphocyte percentage invariably improve more rapidly and consistently than do those in which the percentage of these cells is low. This comparison applies to patients in the same stage of the disease.

2. As the patient improves the percentage of lymphocytes increases directly as the improvement.

3. Progressive failure of the patient is invariably coincident with a decreasing lymphocyte percentage.

4. When the lymphocyte percentage is down to 10 the prognosis is bad; when down to 6 the patient will most probably die within six to ten weeks; when down to 3 death is but a matter of days.

The hemolytic index and lymphocyte percentage go hand in hand, a rising index is coincident with an increasing lymphocyte percentage and vice versa.

Other Cells. The eosinophiles and large mononuclears retain a normal count.

TABLE.

	Moderately advanced cases. White count up to and including 10,000.	Advanced cases. White count from 10,000 up to and including 20,000.	Far advanced cases. White count above 20,000.	All cases. White count from 5000 to 35,200.
Total number of cases	133	412	32	577
Average white count	8500	13,415	25,275	12,339
Average lymphocyte percentage . . .	32.17%	20.8%	18.8%	29.01%
Cases in which lymphocytes were below 30 per cent.	65	258	29	352
Cases in which lymphocytes were above 30 per cent.	65	141	3	209
Cases in which lymphocytes were 30 per cent.	3	13	0	16
Lymphocyte percentage range . . .	7% to 60%	3% to 65%	6% to 40%	3% to 65%

CONCLUSIONS. 1. In uncomplicated cases of tuberculosis the average number of red cells is normal or above excepting during a short time prior to death.

2. The hemoglobin percentage averages about 85 per cent. excepting during a short time prior to death.

3. The red cells exhibit an increased resistance to the hemolytic action of salt solutions, this resistance, as a rule, being increased directly as the progress of the disease.

4. Resistance to hemolysis will probably be found of diagnostic value.

5. The prognosis becomes less and less favorable as the hemolytic index falls.

6. The hemolytic index and lymphocyte percentage bear a direct relationship in prognosis.

7. The total white count increases directly as the disease progresses.

8. In most instances the stage of the disease, in uncomplicated cases, can be more or less accurately determined by the total white count.

9. The polymorphonuclear neutrophils have but little if any phagocytic action in this disease.

10. A high polymorphonuclear percentage makes a bad prognosis.

11. It is strongly probable that the lymphocytes are markedly phagocytic in tuberculosis.

12. A high percentage of lymphocytes is a very favorable prognostic index.

13. The following blood findings are positive proof of improvement in any given case: (a) Decreasing white count; (b) falling polymorphonuclear percentage; (c) rising hemolytic index; (d) rising lymphocyte percentage.

14. Blood examinations should be made coincident with every physical examination, otherwise the physician misses most valuable information relative to his patient's condition.

RELAXATION OF THE SACRO-ILIAC JOINTS AS A CAUSE OF SCIATICA AND BACKACHE:

WITH NEW POINTS IN THE DIAGNOSIS.

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SACRO-ILIAC disease is commonly overlooked by doctors. It is considered to be rheumatism, or more commonly sciatica, and is treated accordingly, mostly by salicylates, hydrotherapy, diet,

lithia water, and electricity. It has nothing to do with rheumatism or uric acid—it cannot be treated by drugs or hydrotherapy. To apply galvanism to compressed nerves is like pouring water on smoke and letting the fire burn itself out. The disorder is common in all walks of life and in people of all ages, save children; in them it is sometimes thought to be growing pains. Laborers get it and treat it better, and protect themselves against it better than do the well-to-do, who accuse themselves of high living and think they have gout. They frequent spas and baths, where the delusion is kept up by doctors who think the same thing. I have known medical men to have it, and they thought that they had rheumatism, and partook of salicylates and avoided meats, beer, and wine.

A prominent neurologist in the Massachusetts General Hospital recently remarked that hereafter all cases of sciatica should be sent to the orthopedic wards before they were sent to the neurological, since he found that at least 90 per cent. of such cases were really sacro-iliac disease, and not any disease of the sciatic nerve. And that is the cause of most nerve pain, both of the back and legs, I have more than assured myself during the past two years. In this time I have seen twenty cases either of sacral backache or of sciatica that were entirely relieved by treating the relaxed or dislocated sacro-iliac joints. All were due to this condition.

Goldthwait first systematized our knowledge of this affection, and it is right to call it Goldthwait's disease. An acquaintance with the anatomy of these joints is necessary before any abnormality can be discussed. They are true joints, the bones are covered with synovial membranes and bathed in synovial fluid.

When we were quadrupeds, and walked on all fours, the joints were firm and strong; but when we reached a higher scale, and walked upright, these joints became vertical, and therefore more unstable than any others. Goldthwait speaks of this articulation as the weakest part of the body, and rightly.

The joint surfaces are large, irregular, and firmly held in contact by ligaments (the greater and lesser sacro-iliac); and indirectly by the muscles of the back and pelvis. They move during every large motion of the trunk, and relax during labor and during menstruation. Motion of these joints always causes play of the two pubic bones, at the symphysis. Not only is it important to remember the structure, but also the relation of the sacral plexus to the articulation.

The upper two trunks of the sacral plexus emerge out of the sacral foramina and pass directly anteriorly down and outward to the lower pelvis into the leg; the gluteal nerves also cross this joint, anteriorly, and any gross or abnormal disturbance in this relationship of the sacrum and ilia causes either pressure on these plexus trunks or else a stretching of them, and this is followed at once by pain in the distribution of these nerves and disability.

The joints themselves are supplied with nerves, and local pain and tenderness is quite a common symptom of relaxation of these joints, due to arthritic strain. The sacrum moves on the ilia on an axis drawn horizontally through the middle. If the upper part of the sacrum is tilted forward on the ilia, the lower part is tilted backward, and the two ilia spread somewhat laterally. If these motions are abnormally exceeded, we have a condition of strain. The function of these joints is largely that of true but limited motion. The pathological changes are those that commonly affect other joints; simple osteo-arthritis, osteomyelitis (septic arthritis), tuberculosis, gout, carcinoma, and, lastly—and infinitely more common—relaxation or luxation of this joint.

That these joints are liable to strain is well illustrated by anybody who stoops for a long time, either in putting on an auto-tire, or over a bed, or who hoes in his garden. The pain in these joints is vastly relieved by straightening up and overextending the back—in fact, overextension is necessary at times to relieve the strained feeling. The guides in Maine who carry canoes, or who paddle them all day in a kneeling position, forestall any strain of these joints and consequent discomfort by wearing a wide webbing belt around the pelvis. This is true of the common laborers with shovel and pick; they support their trousers by a leather belt about the pelvis, just above the trochanters, and at the same time support their back joints. Iron moulders also wear broad belts as protectives.

There may be simple strain and relaxation of the joint ligaments, with some backache, due to auto riding or travel in cars or on horseback; or from lying in hammocks or soft beds with weak springs; or a subluxation may follow a violent trauma directly applied to the back, or strains during football, or wrestling, or from tripping, or slipping, or lifting. Goldthwait mentions the case of a woman who was invalided for thirty-five years after lifting a basket of peaches high up in the air. She felt something slip in her back and was bedridden for years after. Slouching in chairs is also a common cause, as are incorrect methods of walking. I have seen three hard labors followed by this trouble. Sudden slipping while rising from bed, chairs, or out of a bathtub has been followed by an acute luxation of this joint. It may occur in slender, weak women and children; it may affect the athlete with superb musculature.

Lateral curvature of the spine is apt to cause relaxation of these joints.

The symptoms are, first of all, backache, especially when lying on the back or on stooping, tender sacro-iliac joints, pain in the sciatics or buttocks, parasthesias in the feet and knees; often lameness and even atrophy of the leg or legs; inability to rise out of low chairs and out of bed quickly; resting in chairs or seats with the

back supported with cushions. In women this is worse during menstruation. The uterosacral ligaments insert in the region of the joint, and these become congested during menstruation and cause relaxation. It is a common cause of backache after operations. It may invalid people by reason of the pain.

The diagnosis is established by various manœuvres. First, it is most important to exclude actual joint disease with tissue change. After this, if there is localized pain on pressure over one or both joints, due to acute arthritis, pain in the legs, numbness, tingling in the toes or heels, we must move the joint in various ways. First, have the patient rise, if he can, out of a low chair; if he has the true joint relaxation, he holds his back stiff and does not bend gracefully, but pushes himself up with his arms and finally, with much effort, staggers to his feet. His back may be arched, and he stoops often when standing. An examination of the back—and this must always be done—shows frequently a straight lumbar spine, and not the normal lumbar lordosis. This is found in severe cases among laborers. Merely standing for a long time in a constrained position may cause joint sprain.

Limitation of motion can be shown by getting the patient to bend sidewise from the hips; one side will be more limited than the other if there is a true relaxation or luxation, although Goldthwait has shown that there is rarely unilateral relaxation. Even in bilateral disease one joint is worse than the other and causes most symptoms.

If the patient is laid on his back and the thigh flexed on the body, it is impossible then to flex the leg on the thigh, as in Kernig's test, without causing pain in the sacro-iliac joint on the same side. The hamstring muscles pull on the ischium, and this disturbs the bone relations of the tender joint and causes pain.

Grasping the crests of the ilia and separating them or drawing them together, causing a disturbance in the relationship of the bones of the joint, brings about sharp pain. Goldthwait's test consists in having the patient stand on one foot and then flex the thigh with the leg extended; during this last the surgeon must put one hand over the suspected joint and the other over the symphysis pubis. The latter will move with each motion of the leg. This, Goldthwait says, always occurs in sacro-iliac relaxation. And because there is greater natural mobility of this joint, there is more tendency to the relaxation. These occur *pari passu*. Then have the patient lie face downward on the bed and grasp the foot on the affected side and forcibly hyperextend the leg; this causes acute pain in the joint, and a corresponding limitation of thigh excursion on that side from pain.

I have modified Goldthwait's test by having the patient lie face downward on a table or bed. Then the examiner should slip one hand under the patient and firmly press the pubic bones, at the same time the leg on the affected side should be moved up and

down. Preternatural mobility of the pubic joint caused by the loose and relaxed sacro-iliac joint is easily detected. In this way the mobility of the pubic joint can be found more easily, because the patient is more steady.

Finally, in case of doubt, a radiogram should be taken of the pelvis, and the difference, if any, of the two articulations noted. In general practice it is absolutely imperative that every obscure joint condition, from rheumatism to dislocation or fracture, should be radiographed. This joint is, however, hard to photograph, and artefacts interfere greatly with a positive result.



FIG. 1.—Relaxation of left sacro-iliac joint, as shown by the diastasis of the symphysis pubis and the widening of the joint at J J and the difference in the A B C angle in the two sides. Radiograph outlined with ink.

On studying several skiagrams in this disease I found that the pubic bone was higher up on the affected side than on the other in cases of unilateral relaxation. This was more marked than the actual luxation of the ilium or the sacrum. This observation that the whole os innominatum is thrust slightly up and back, the pubic portion of it being the distal end, as it were, of a lever; at this end the motion is greater than at the sacral end.

Relief from pain by posture is often a sign of this disease. Goldthwait mentioned a doctor who could not sleep unless his thighs were tied together. When he slept, if his knees were separated,

his joints relaxed and he had intense pain, because his ilia, being pushed apart by the thighs, caused joint strain at the sacro-iliac junction.

By producing the normal lumbar curve, either by pillows under the back when lying down or by lying face down between two chairs, if there is relief from pain, there is further evidence of relaxation of this joint. Sometimes by palpation the ilium on the affected side may be felt to be too far back or forward by comparison with the opposite one—this is rather a difficult thing to do for the untrained. Frequently in severe cases the patient may be bedridden or limp markedly.

Having then established the fact that the normal joint relationships are disturbed, we must reduce the luxation and keep it reduced. This is accomplished in several ways, first by posture and correction of improper attitudes of standing and sitting. If the case is a slight one, have the patient lie with a pillow under his lumbar vertebræ, or else between two chairs, face downward. The joints, if really dislocated, may require anesthesia and forcible reduction and immobilization with a plaster cast. Generally the application of adhesive straps over the dorsum of the pelvis is sufficient. To do this have the patient stand up and then apply the end of an adhesive strap to the skin, just under the anterior superior spine; then very forcibly apply the plaster to the back, having the patient turn away from the surgeon; put on four straps reaching from the anterior spines down to the top of the trochanter and the top of the intergluteal fold. This generally gives immediate and very gratifying relief. Straps worn for six weeks will often completely cure a very bad case. Sometimes it is necessary to encircle the pelvis. One must be very careful not to have the straps come up too high, or else there will be some tilting of the ilia forward, and more relaxation and more pain.

A wide belt made of webbing nine inches wide, extending from the trochanters up to the crests of the ilia, and encircling the pelvis and buckling in front, gives great relief by immobilizing the joints. Perineal straps are needed in such belts—they are necessary to keep it in place.

Dr. Wm. J. Merrill, of Philadelphia, has devised a very efficient and ingenious brace, which consists of a pad over the sacrum, and shaped like it; it may be compared to a reversed truss with the pad over the back and not in front over the hernial rings. Upon this are four arms that encircle the pelvis to the anterior iliac spine. Two are on either side, and the upper and lower bands meet below the spine, and then the junctions on either side are held by a strap crossing the lower abdomen. These side arms are fastened to the sacral pad by flat springs. This apparatus is covered with soft leather and is easily worn, is comfortable, and requires no perineal bands to hold it in place. In three of my cases it was most efficient;

not only was it of great benefit to the patient, but was comfortable and did not get out of place. To make an accurate fit it is necessary sometimes to make a cast of the back, and then to mould the brace over this cast. It must be remembered that cases are prone to relapse.

The following cases, occurring in general practice, illustrate the various grades of this affection and the various ways of acquiring and of curing it.

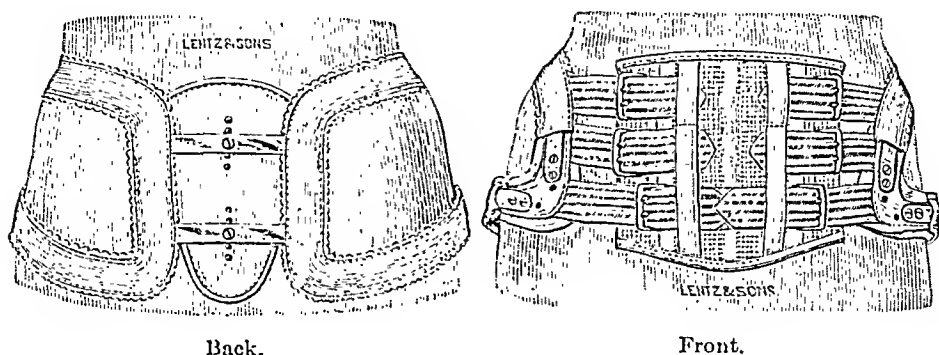


FIG. 2

CASE I.—J. W., a slender, middle-aged man of slight musculature, suffered much pain in his buttocks, which he thought was neuritis. This pain was aggravated by stooping, especially in putting on automobile tires. His lumbar spine was straight and his sacro-iliac joints relaxed. In putting him in a position of exaggerated lordosis, his pain at once left him. A webbing belt completely relieved him of all pain. He was forbidden to lounge in his office chair, and was ordered to support his back while auto-riding.

CASE II.—T., a tall, slender man, aged fifty years, limped into my office with sciatica. He had been treated for months by salicylates and drugs. His right sacro-iliac joint was markedly relaxed. He never could get out of bed during the past six weeks without help, but when once on his feet was fairly comfortable. By applying a belt and lordosis exercises he was completely relieved in about three days' time, and was cured in a month's time. Lounging in an office chair caused his relaxation.

CASE III.—Mrs. D., a young slender woman, the mother of three children, after the birth of the last—a twelve-pound boy—found that she could not rise out of bed in the morning except her husband lifted her bodily and put her on her feet. Her right joint was markedly relaxed; her backache, especially at her menstrual epoch, was very severe; she was nervous and inclined to be hysterical. Her bed, I found, was a very old spring mattress that yielded to the slightest pressure, and, in fact, where the patient lay was a deep depression in the springs. Her relaxed back came from a very hard labor and lying in a bed that sagged so much that her

sacro-iliac joints, being unsupported, gave way completely. Adhesive straps applied for a month completely cured her.

CASE IV.—Mrs. R., a young slender mother, suffered exceedingly from pain in her back after labor. Her pelvis was normal as to its contents, but her sacro-iliac joints were very tender, and Goldthwait's test caused her some increase in pain. Strapping and bandaging did very little toward relieving her pain—in fact, the only way in which she had any comfort was to lie in bed all day, with a pillow under her lumbar spine. After a year's effort by me, she obtained complete relief at the hands of Dr. Merrill, who applied one of his braces to her pelvis. Childbirth and an unnatural way of holding herself with the abdomen drawn in, in order to have a flat stomach, was the cause of her backache.

CASE V.—Mr. D., a grocer, a large, strong man, suffered much with his back. On examining him I found that he was unable to rise from an ordinary arm chair, without great effort and pain, and after arising he placed both hands over his sacrum and groaned. Various tests soon showed that he had relaxed joints and a very straight lumbar spine. He was in the habit of lifting heavy barrels into his wagon, and frequently suffered from pain in his back for hours afterward. Riding in his wagon on a seat without a back caused him constant pain. After much effort he was finally cured by the exaggerated lordosis posture between chairs. A belt seemed to tilt his sacrum so that his pain was increased; and strapping gave him no relief. He said that the hyperlordosis position gave him the greatest ease and final cure.

CASE VI.—A nurse in the Germantown hospital, a tall, large woman, frequently lifted a patient with appendicitis out of bed to a stretcher. Her back caused her much trouble, so that she was miserable most of the time. She could not with any comfort stand erect, and stooped quite markedly. After a night's journey in a sleeping-car berth she suffered so much from backache that she was unable to rise, and had to be lifted out by the porter and her friends. An extremely straight back and tender sacro-iliac joints were found; she could not lift her extended leg higher than a foot without causing her great pain in the corresponding sacro-iliac joint. A webbing belt worn for a month completely cured her. No doubt the strain of lifting, and the ride in the sleeper in a soft bed, causing the joints to relax more, was the cause of her extreme disability.

CASE VII.—Mrs. G., after a pelvic operation, suffered greatly with sacral backache. She was a neurotic woman, worn out with childbearing and the care of a large family. Goldthwait's test caused much pain in her joints, which were tender to the touch. Her pain was aggravated by riding in trains, and to secure any comfort she was compelled to brace her back with cushions, etc. She had sciatica during train riding, and parasthetic sensations

in her toes. Strapping helped her some—a belt did more; but cure was not effected until Merrill's brace was applied. The relaxation during ether, on a flat table, no doubt caused her joint ligaments to relax and her back to flatten, causing pain by pressure on the sacral plexus, from subluxation.

That sudden and total disability from the luxation of this joint can and does occur is illustrated by the following case:

CASE VIII.—Mrs. A., aged thirty years, mother of one child, had, after labor (a difficult and trying affair), a great deal of pain in her back and along the sciatic nerve on the left side. A completely torn perineum and cervix, and retroflexed uterus, led me to think that her backache was due to her uterine condition. Accordingly, a gynecologist effected a very skilful repair, and for a time the pain disappeared. While lifting her baby out of a crib she was seized with violent backache and sciatica. Examination showed that her left sacro-iliac joint was exquisitely tender, and the ilium on that side projected farther back than did the right one. Various tests all confirmed the diagnosis of subluxation of the left sacro-iliac joint, and she was strapped, then bandaged, with very little relief. Her nights were wretched; she could not turn or move without exquisite pain in her back and thigh. Pillows under her spine helped her somewhat, but complete cure was not obtained until a cast was made of the dorsum of her pelvis and Dr. Merrill, who did this, applied one of his braces, which effected great relief, and finally a cure.

I might enumerate a dozen more cases that I have seen among carpenters, sailors, and laundrymen, all of whom were crippled with sciatica, and who were relieved by postures, exercises, and fixative apparatus. I have demonstrated to people the cause of their disability and probable means of cure by encircling their pelvis with my own leather belt, applied low down and tightly, above the trochanters and over their clothes. All at once said that this simple measure gave partial but immediate relief.

These cases illustrate the futility of treating at least a portion of sciatica cases with drugs or any other measures save orthopedic ones. Having seen within two years twenty such cases in general practice and in hospitals, I am led to believe that true neuritis or neuralgia (idiopathic) of the sciatic nerve is a rare clinical entity. It may be due to reflex causes, such as constipation, pelvic tumors, etc., but it is hard to believe that actual degeneration of the sciatic nerve is a common thing.

PNEUMOCOCCUS PERITONITIS.

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AFTER the full development of the surgery of the appendix, it was the opinion generally felt and often expressed that acute peritonitis was always due to an inflammation of the appendix, or the pelvic viscera, or a perforative lesion of one of the abdominal viscera, or of the abdominal wall. As experience increased, however, cases of acute peritonitis occasionally occurred in the experience of many surgeons which could not be accounted for by any of these causes. Reports followed by several surgeons, of a small series of cases of acute peritonitis from "unknown sites of infection,"¹ or "without demonstrable lesion."² These and the cases related by other surgeons in the discussion of such reports were in many instances due to streptococcus infection, others to *Bacillus coli*, and in other cases no bacteriological examination was made. The larger number of such cases, however, have been examples of pneumococcus peritonitis. Thus, in 1903, Jensen³ collected and reported 106 cases (adults 48 and children 58), and many have been reported since. In 1906 Annand and Bowen⁴ collected 91 cases below fifteen years of age. In fact, the greater number of the cases have occurred among children, and with few exceptions among girls. Thus, among 74 cases collected by v. Brunn⁵ in 1903, 57 were under fifteen years of age, and in 1906 Ashdowne⁶ could only collect 31 cases among adults.

My interest in this subject was aroused by two cases of pneumococcic peritonitis which occurred in my service at the Presbyterian Hospital during the last year (1909), one in a girl, aged seven years, the other in a woman. I have made no attempt to collect all the cases reported since Jensen's paper in 1903, as the results would not justify the labor required.

The peritonitis may be a part of a pneumococcic septicemia, with multiple foci of infection, but more often it is (1) secondary to another local pneumococcic focus as a pneumonia, empyema, etc., "secondary cases," or (2) it is the first point attacked by the organism, "primary cases." Annand and Bowen⁴ found the latter variety were more common among children in the proportion of 47 to 30, while v. Brunn⁵ states that the secondary form is more common than the primary, but Annand and Bowen have placed 14 cases, whose classification was doubtful, in a third class.

The etiology of the peritonitis is a matter of the greatest interest. Among the secondary cases the primary focus is pulmonary (lungs or pleuræ) in the great majority of cases (73 per cent.³). Next in

frequency comes otitis media and throat infections. In cases secondary to pulmonary lesions does the infection reach the peritoneum through the blood or by penetrating the diaphragm? There is no evidence of the latter course. When the diaphragm has been examined microscopically, pneumococci have been found in one case in the pleural serosa and subserosa, and in a second case all through the diaphragm. But this case was one of pneumococcic septicemia with abscess of the shoulder-joint and endocarditis, and the organisms were certainly in the blood. Experimentally in animals to secure penetration of the diaphragm by the organisms, it is necessary to use virulent cultures and to destroy the pleural endothelium by chemical irritants. Even then no peritonitis results. In the diaphragm, it is to be remembered the lymph current is away from the peritoneum. In cases secondary to otitis or a throat lesion, direct extension is out of the question. As it is established that in pneumonia in man pneumococci can be grown from the blood in nearly every case (Ewing), the presumption in favor of the peritoneum being infected through the blood in such cases is very strong, and is generally accepted by writers on the subject. Another explanation is also possible, and as it offers an explanation of the great preponderance of cases in children (and women too), the writer suggests it, though he has seen it nowhere mentioned. The sputum in cases of pneumonia is often swallowed in whole or in part, regularly by children, who seldom expectorate, and more often by women than by men. Pneumococci do not grow in acid media, and though they may normally be killed by the gastric juice, reduction of its acidity in disordered digestion may allow them to reach the alkaline small intestine. Of the 23 cases of diffuse pneumococcic peritonitis in adults collected by Ashdowne,⁶ there were affections of the stomach in 5 (perforating ulcer in 3, chronic ulcer in 1, carcinoma in 1), indicating that the infection probably occurred from the stomach contents in these 5 cases. Numerous cases of enteritis in adults due to the pneumococcus are recorded, sometimes associated with peritonitis, and Jensen³ mentions 2 cases in children. It has been found in a swollen Peyer's patch in a primary case.⁴ Jensen,³ experimentally, obtained general fibrinopurulent peritonitis and found pneumococci diffused through the gut wall in one of two young rabbits that were given 10 c.c. of a virulent culture of pneumococci. The appendix was affected in 3 of the cases collected by Ashdowne,⁶ and a number of such cases have occurred, especially in adults. It has been definitely established and accepted that the infection may and does occur from the gastro-intestinal tract in primary cases, and the condition of this tract appears not to have been investigated in secondary cases. The same explanation applies in cases where the primary focus is in the throat or middle ear, which drains into the throat, whence the discharges may be swallowed, but

it does not apply in the two cases mentioned by Annand and Bowen, where an intermuscular abscess was the primary lesion.

But though this explanation might account for the relatively large number of cases occurring in children, it does not explain why such a large majority occurs among female children. In considering the etiology of primary cases, Jensen³ gives the possible avenues of infection as follows: Through the abdominal wall (penetrating wounds, etc.); through the diaphragm (from the pleuræ); from the blood; through the intestinal canal; through the genital organs, and from other abdominal organs. In the primary cases one of the most likely channels is the alimentary canal. This has already been referred to above. Bryant⁸ suggests that the diarrhea, so often present, may be an evidence of gastro-enteritis, which would determine the passage of living organisms through the stomach into the bowel and then through the wall of the latter. Quervain⁹ reported a case of pneumococcic peritonitis in a child where five months later the appendix on removal was found to contain pneumococci. On the basis of this, and another case quoted from Krogius, Quervain thinks the appendix the commonest source of origin of the peritonitis in primary cases. Although such an etiology is somewhat more common in adults than in children, there is no evidence to prove that it is more than an exceptional one. Of the 91 cases collected by Annand and Bowen, 73 per cent. of all cases, 84 per cent. of the primary cases, and 67 per cent. of the secondary cases were females. Both of the writer's cases were females, and all who have collected series of cases give a very similar result. These striking figures are very difficult to account for. They suggest as an important etiological factor the female genitals, especially as we know that they are the regular channel of infection in gonococcic and tuberculous peritonitis in the female. But there is very little pathological support to this theory. In one case recorded by Lop⁶ the peritonitis followed delivery, and pneumococci were found in the lochia. Annand and Bowen⁴ mention two cases where a congested tube was found, one where there was a slight vaginitis, another where there was slight vulvitis. It is possible that the pneumococci may pass through the tubes, causing but little local reaction, just as in a case of diffuse pneumococcic peritonitis the intestines may show comparatively little congestion, but, however strongly suggested by the figures given above, it must be admitted that there is singularly little pathological proof of the genitals being the common channels of infection. It is quite possible that in some cases the pneumococci have entered the circulation through an apparently intact mucosa and found in the peritoneum conditions favorable for development. In not a few cases the peritonitis and pneumonia occur so closely together that it is difficult or impossible to say which is the primary lesion. Jensen³ found experimentally in animals that pneumococci injected into the peritoneal cavity were

found in the blood in every case within a few minutes, four to five at the earliest. If the animals live long enough, the pneumococci diminish in the blood and eventually disappear if they recover. Thus, in a pneumococcic peritonitis, the lungs may become infected by the blood stream, and the reverse also occurs.

Clinically as well as pathologically two types are distinguished, the circumscribed and the diffuse forms. The difference is one of degree only; the circumscribed form sets in acutely, but passes into a subacute or chronic stage as soon as the pus becomes encapsulated. This tendency to the encapsulation and limitation of the process depends upon a characteristic feature, the formation of a fibrinoplastic exudate, which forms a false membrane and tends to localize the process. In the diffuse form there is less fibrinoplastic exudate; the pus is not encapsulated, the acute symptoms persist, and it does not differ essentially from other varieties of diffuse peritonitis. Either of these types may be of the primary or secondary variety; hence we may distinguish four varieties. My experience is limited to the diffuse form.

The characteristics of primary diffuse pneumococcic peritonitis are the acuteness of the onset and the severity of the symptoms, intense pain, vomiting, diarrhea, and prostration, passing on to the terminal symptoms of peritonitis if unrelieved by operation. The temperature, pulse, and leukocyte count are all high; there is general abdominal tenderness and rigidity, which may be more marked below the umbilicus or even in the right lower quadrant. There may be tympanites, with dullness in the flanks; in fact, the signs are those of a diffuse septic peritonitis.

In the secondary diffuse form the onset of the peritonitis and its signs and symptoms are marked enough in about half the cases (47 per cent.⁴) to point definitely to its presence. In the other cases the primary condition or the presence of a severe general infection (in nearly half the cases), as indicated by multiple lesions (pericarditis, etc.), so obscure the local manifestations as to prevent their clinical recognition. When the peritonitis has been diagnosed in these cases its symptoms and signs have been for the most part the same as in the primary form.

In the primary circumscribed form the onset is acute with abdominal pain, possibly localized at first, but soon becoming general, vomiting, at first or for some days, and diarrhea, which is more persistent. The fever and other constitutional symptoms, as well as the local ones, characterizing the first stage, subside in ten to fourteen days. In this form the inflammation becomes encapsulated by adhesions and the fibrinous character of the exudate, so that in the second stage we have the formation of an intraperitoneal localized abscess. This is usually subumbilical, and rather more to one side than mesially. During this stage there may be constipation, the patient emaciates, the lower abdomen swells, and there is slight rise of

temperature. At times the general condition remains good. If unrelieved, the abscess tends to perforate a month or so after the onset, and usually at the umbilicus. By this time the cachectic and emaciated appearance and the distended abdomen suggest tuberculous peritonitis.

In the secondary circumscribed form, as in the secondary diffuse form, the primary infection may mask the onset of the peritonitis if the latter sets in immediately after the onset of the primary infection, or if the latter is merely the first local manifestation of a pneumococcic septicemia. Otherwise and in its second and third stages the secondary is the same as the primary circumscribed form. In the 91 cases collected by Annand and Bowen,⁴ 21 were of the primary and 19 of the secondary diffuse forms; 26 were of the primary and 11 of the secondary circumscribed forms; while 14 cases were unclassified.

DIAGNOSIS. From the above brief summary of the clinical manifestations of pneumococcic peritonitis it will be observed that there is little that is distinctive about the disease to distinguish it at the outset from an appendicular or perforative peritonitis. The pain is often referred to the right lower quadrant more than to other regions of the abdomen, and in appendicitis in children, in whom pneumococcic peritonitis is most prevalent, the pain is often not well localized, particularly in the early stages. Diarrhea is a very constant accompaniment of pneumococcic peritonitis, whereas constipation is the rule in appendicitis. But here again we find that diarrhea is not at all uncommon in appendicitis in children, in whom pneumococcic peritonitis is relatively most often found. Diarrhea is also a not uncommon accompaniment of peritonitis due to a pyosalpinx or a pelvic inflammation. The fact that pneumococcic peritonitis occurs most often in children and in females and that it is regularly accompanied by diarrhea, are the only distinctive features to assist in the diagnosis. If my first case is not an exceptional one, the leukocyte count may be of assistance in the diagnosis, for in this case it was very high, 67,000 (polymorphonuclears, 94 per cent.). In the second case, however, it was only 19,000. The high count in the first case may have been due to the pulmonary condition which soon manifested itself. In spite of all slightly distinctive features, the acute diffuse form is almost always operated on for appendicitis or a perforative peritonitis. Michaut¹⁰ stated, in 1901, that whereas the diagnosis has frequently been made in the encysted form, it has only once been made in the diffuse form.

The secondary diffuse form is no easier of diagnosis, for in more than half the cases its onset is obscured by the symptoms of the primary infection or by other secondary lesions. The history of the case and the fact that peritonitis is one of the commonest, if not the commonest secondary lesion in pneumococcic infections, espe-

cially in female children, is often the only clue we have. Hence the importance of the history in the secondary cases.

In the circumscribed form, unless the history of the acute onset, or, in some cases, of the previous pneumococcal infection is obtained, the diagnosis is not likely to be made until the appearance of the localized abscess. Sometimes it has not been made until the latter bursts, or is on the point of bursting.

As in the secondary diffuse form, so in the secondary circumscribed form, the diagnosis may be obscured by the primary lesion so that no diagnosis is made until an encapsulated abscess forms.

At the time of operation the gross pathological character of the pus is sufficiently marked to suggest the diagnosis, for the pus is odorless, yellowish, or greenish yellow, and is distinguished by fibrinous flakes or masses in the pus, and on the bowel. In some cases a secondary infection with *Bacillus coli communis* may give the pus an odor, and the amount of the fibrinous exudate varies, being less abundant in the diffuse cases.

While, on the one hand, it is necessary to diagnosticate cases of pneumococcal peritonitis which are secondary to pneumonia, etc., on the other hand there are cases of "delayed pneumonia," in which all the symptoms point at first to peritonitis, such as that due to appendicitis, although there may be no actual peritonitis present. Such a case should be carefully considered to avoid an unnecessary operation. An example of this class of cases also occurred in my service during the previous year, and was as follows:

Miss W. F., aged twenty-four years, single, was admitted to the Presbyterian Hospital February 18, 1909. For five months she had felt badly, with persistent drowsiness, constant headache, and loss of appetite, though she feels hungry. She is apt to vomit after breakfast, and has palpitation and shortness of breath. No loss of weight. Leucorrhea for last three months, for which she had used a vaginal douche with a dirty tip. Five days ago she contracted a severe cold. She coughed a great deal, and raised much thick, yellowish sputum, and vomited after severe coughing spells. For last three days she was more acutely ill, with high fever, chilly sensations, severe headache, vomiting of everything eaten, and languor. Some general abdominal pains. Bowels had not moved for three days.

Examination. A few inconstant rales in both apices, harsh breathing in right apex. Abdomen tender all over, especially in right lower quadrant, with well-marked tenderness at McBurney's point. Slight rigidity; no masses felt. Rectal examination shows right-sided tenderness. Neck somewhat rigid. Muscles of calves and thighs extremely tender. Urine negative. After admission the temperature ranged between 104° and 106° for the next three days. The leukocyte count rose from 12,500 (polymorphonuclears, 97.5 per cent.) on February 19, to 21,700 on February 20, and

23,700 (polymorphonuclears, 95 per cent.) on February 22. On February 20 Widal reaction was negative, blood culture was sterile, and there were no malarial plasmodia. On February 22 smears from urinary sediment show staphylococcus, and a culture from catheterized specimen gave a pure growth of *Bacillus coli*. The urine now contained albumin (3.1 per cent.), a trace of indican, pus, and red blood cells. A hematogenous renal infection was thought of in connection with slight pain and tenderness over the right kidney and the urine analysis. The patient was seen by the house physician, and then by the attending physician, who declared that there was nothing in the lungs. The cough bothered her considerably. The bowels were loose, moving eight to nine times a day; the movements were greenish. The patient was very prostrated and irrational at times. I was confident that there was no appendicitis, though the pain and tenderness in the right lower quadrant continued to be the only local signs. On February 22 a tender mass was felt in and to the right of the median line, in the hypogastrium. In order to determine if possible, the cause of the symptoms, an exploratory laparotomy was made. The mass felt was found to be the distended bladder, though she had been catheterized a few hours before. The appendix, peritoneum, and all abdominal organs were found negative. After operation the temperature fell somewhat (to 102°), but the following day the pulse rate rose to 140; she began to be dyspneic and cyanosed, and beginning consolidation was found in the right upper lobe. She was transferred to the roof and to the Medical Service, but failed to respond to stimulation, and died February 24, at 7.30 p.m. There was no autopsy allowed, but all the signs of a frank pneumonia were present. I have also seen cases of acute appendicitis in young adults in whom the early symptoms were referred to the right thoracic region. This is not uncommon in children, in whom the reverse is still more common, that is, pain referred to the abdomen in cases of pneumonia.

PROGNOSIS. Whether the peritonitis is primary or secondary does not appear to affect the prognosis, according to Annand and Bowen,⁴ but the latter does depend upon whether it is diffuse or encapsulated, whether or not it is operated upon in due time, and whether or not there are other severe complications. Of 46 cases of diffuse peritonitis in their table, 18 were operated upon, with a mortality of 66.6 per cent. while all those not operated upon died. The total mortality of the diffuse form was, therefore, 86 per cent. Of 45 cases of circumscribed appendicitis, 44 were operated upon, with a mortality of 13.9 per cent. An early and correct diagnosis followed by a prompt operation will favorably affect the prognosis.

TREATMENT. The treatment is surgical. Early operation affords the best prognosis. The operative treatment is the same as that of other varieties of diffuse or circumscribed peritonitis, except that

there is usually no portal of infection that requires removal or local treatment. In most cases the operation will be undertaken without an accurate diagnosis. If the pus is odorless, flocculent, greenish or yellowish green, and without free gas, the viscera need not be searched for a perforation. The appendix will probably have been examined, and it is very desirable to examine the pelvic viscera to determine the etiology. In the acute diffuse form, Annand and Bowen think that mopping out the pus and closing the incision without drainage appears the wisest course. It is probably better for each operator to follow the technique he is accustomed to in acute diffuse peritonitis from other causes. Personally, I generally employ drainage. In the encapsulated form the operation merely consists of opening and draining a localized intra-peritoneal abscess. The following is the history of the case of acute pneumococcic peritonitis upon which I operated:

M. C., a girl, aged seven years, was admitted to the Presbyterian Hospital January 30, 1909. One week before, she began to have sore throat, cough, abdominal pain, fever, anorexia, and diarrhea.

January 28 she had sudden abdominal pain and tenderness in the entire lower abdomen, and vomited almost all day. The following day there was no vomiting, but the pain and tenderness continued.

On admission the abdomen was somewhat distended, symmetrically, and showed much restriction of the respiratory movements. The abdomen was everywhere rigid and tender, especially in the right lower quadrant. Percussion was tympanitic everywhere, except about McBurney's point, under which there was the sense of a mass, and in both flanks, where there was shifting dullness. Lungs: breath sounds exaggerated over both upper lobes in front; there was dullness over the right base posteriorly and over the outer part of the right scapula. The breath sounds were diminished over the base. Temperature, 104°; pulse, 100; respiration, 56; leukocyte count, 67,000 (polynuclears, 94 per cent.); blood pressure, 85.

On the diagnosis of a diffuse peritonitis probably due to appendicitis, she was operated on at once, January 30, by the usual muscle-splitting incision over the appendix. The latter was retrocolic and normal, but was removed. The peritoneal cavity was filled with an odorless yellowish seropus, with fibrinous flakes, thicker and more yellow in the pelvis. No perforation in the ileum, and the mesenteric nodes were not enlarged. Through a median epigastric incision the stomach, duodenum, and gall-bladder were examined and found normal. There was only a little pus above the transverse colon. No cause of peritonitis found. Drain to pelvis. Upper wound closed. Infusion of 500 c.c. normal saline solution given on table. Patient in Fowler's position and enteroclysis given, but not well retained.

Culture of pus showed pure culture of pneumococcus. February

2, signs of consolidation at right base; also bronchial breathing at left base. Croup kettle employed. Slight distention relieved by enemata. Irrational much of time. February 6, temperature, respiration, and pulse lower and dyspnea less. Fowler's position stopped on third and enterocolysis on fourth day. Still has frequent loose dejections, with mucus. She is more rational. Coughs a great deal, and as a result the median abdominal wound has begun to open up. Only a slight shreddy purulent discharge from the lower wound. February 8, temperature has been down to 99.4° , but is up again to 103.5° . Consolidation on both sides to near angle of scapulæ. Pulse and general condition slightly improved. Ten c.c. of Hiss' serum was given on February 9, and the following morning she was moved to the roof and the croup kettle stopped. Twenty c.c. of Hiss' serum was given during February 11. The lower wound discharges moderately. Temperature fell gradually to 99.8° on March 1, then rose to 102° on March 3, when a mass in right lower quadrant, at lower angle of wound, was opened through the wound and several ounces of foul pus evacuated. March 13, upper wound practically closed. On March 17 the patient commenced to vomit, and continued to for three days. Bowels constipated, but moved to enemata. Some cramp-like pains were present and a mass was felt in left lower quadrant. Obstruction feared, but symptoms decreased and patient felt well again, though a definite but smaller mass was still palpable April 1. On her discharge, April 10, there was a well-marked hernia in upper wound. Except for the latter, she was in fine condition when presented to the New York Surgical Society on April 28, 1909.

In April, 1909, another case was brought into the hospital in a moribund condition. Mrs. K. had had for five years a tender spot just above and to right of umbilicus. No other symptoms suggestive of gastric ulcer. Five days ago at 2 P.M., she was suddenly seized with terrible cutting pain about the umbilicus, lasting five minutes, followed by general but less severe abdominal pain. She had a chill with the onset, vomited soon after, and has been prostrated since. The vomiting has persisted almost continuously. She was distended, and belched much gas. Daily enemata, with scant results. Bowels involuntary today. Temperature 105° three days ago.

On admission she was in collapse, with a cold, clammy, mottled surface and almost pulseless. Lungs negative anteriorly. The abdomen was moderately distended, tympanitic, except in flanks, where there was shifting dulness, especially on right side; tender all over, especially in lower half, but not rigid. Peritonitic fascies. Pelvis: laceration of cervix and perineum; menstruating; leukocyte count, 18,000 (polynuclears, 87 per cent.); temperature, 100.4° ; pulse, 160; respirations, 36. As she did not respond to stimulation, operation was out of the question, and she died within a few hours.

On autopsy, abdominal organs were normal and presented no perforation. Lungs normal. There was a diffuse peritonitis, with a greenish-yellow, flaky, purulent exudate. Culture gave a pure growth of pneumococcus.

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FREUD'S PSYCHOLOGY IN ITS RELATION TO THE NEUROSES.

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IT is the distinction of Freud's teaching with regard to the neuroses¹ that it contemplates immediately the psychology of these disorders and traces their origin to psychic mechanisms involving principles elsewhere inherent in biology, and having as elsewhere an economic significance. Freud's conceptions are essentially a restatement of biology in psychological terms. The functional aspect of organic process is the dominant theme of his psychology.

Working alone for many years, his views at first met with scant hospitality, but it now seems safe to predict that Freud's teaching, vigorously furthered by the researches of Jung and the Zürich school, is destined for a leading role in the future development of psychopathology.

In his method of study, which sought the etiology of the neuroses in intrinsic, psychological determinants, Freud has faced the problem squarely. Imputing a psychological source to these conditions, he has gone to the heart of the situation in the effort to trace their embryonic development.²

¹ In these columns the term "neurosis" is employed in lieu of the less wieldy "psychoneurosis" to indicate the disorders of function embraced under the terms "hysteria," "psychasthenia," so-called "neurasthenia," and related conditions.

² Freud, *Drei Abhandlungen zur Sexualtheorie*, 2d ed., Deuticke, Vienna (Translation by Brill). *Sammlung Kleiner Schriften zur Neurosenlehre*; vols. i and ii, Deuticke, Vienna. *Analyse der Phobie eines fünf-jährigen Knaben*; *Jahrbuch für Psychoanalytische u. Psychopathologische Forschungen*, Band i, Deuticke, Vienna, 1908.

To this end Freud selected hysteria as the appropriate paradigm of the neuroses, and applied himself to a detailed analysis of this disorder. As the import of this rigorous study, entailing years for the adequate analysis of a single case, is not generally appreciated, a rough outline of its principal results will, perhaps, not be amiss. Besides, even the most hasty sketch of Freud's views must perforce take account of their inception, for their logical account traces also the course of their historical development. Here the clinical aspects alone are contemplated, abstracting as far as possible from the broader biological implications of Freud's conceptions. To treat even meagerly these wider issues would require the space of a separate paper.

As a pupil of Charcot,³ Freud early became aware of the psychic nature of hysterical shock. For Charcot, it will be remembered, was the first to recognize that in this phenomenon the clinical picture is not due to the physical injury *per se*, but to the psychic disposition induced by the sudden and violent nature of the provoking incident. Hence, Charcot taught that hysterical shock consists essentially in a psychic dissociation—that, owing to the concomitant affective state induced by the violence of the inciting event, the group of images momentarily occupying consciousness is so heightened in intensity as to persist independently of normal association with the images occurring subsequently. Thus, in the vividness of the momentary impression, a fragment of the personality is denied participation with the remainder of the ego, and it is the persistent preoccupation with this dissociated group of images which constitutes hysterical shock. Following this tack, Breuer and Freud⁴ applied themselves to the epoch-marking study of hysteria which was reported in 1895.

These authors set themselves the task of unearthing the source of hysterical symptoms by means of a searching inquiry into the innermost experiences of their patients. It should be said that in this inquiry, Freud, following Breuer, resorted to hypnotism in varying degrees in order to facilitate the reproduction of the patient's unconscious imagery, but in the technique which Freud later adopted hypnosis was abandoned, as the method of "free association" in the waking state proved equally efficacious.

We shall here mention only the most striking results of this conjoint research, in which are laid the foundations of the principles of psychic analysis, which later culminated in Freud's present system of psychology. For a fair appreciation of its import one must, of course, refer to the original work with its detailed analysis of selected cases. Perhaps of chief theoretical value was the discovery that the primary factor lay far beyond the recognized and—if one may venture a paradox—far beyond the unrecognized

³ Charcot, *Leçons sur les Maladies du Système Nerveuse*, 1885.

⁴ *Studien über Hysterie*, 1910, 2d ed., Deuticke, Vienna.

experiences of the patient. In traumatic hysteria, in which the original occasion is hallucinated in the hysterical attacks, the causal connection is obvious, but in other manifestations it is by no means so clear. However, Breuer and Freud found that the most diverse hysterical symptoms, *e. g.*, neuralgias, anesthesias, phobias, etc., may all be referred to an analogous etiology. Frequently the connection between the morbid event and the resulting symptom presents a quite transparent, logical relation, as in cases in which persistent vomiting manifests itself as the result of a repressed painful emotion experienced at table. In other cases, the connection between the imputed cause and the symptom it occasions has only a symbolic significance, where, for example, vomiting ensues at the instance of a moral revulsion or in the resistances of pregnancy.

From this larger view of the etiology of the neuroses the writers extend the conception of "traumatic hysteria" to a wider application, for, after all, the real trauma is the *psychic* insult. So that any event involving a sufficiently painful affect may constitute a psychic trauma, or a summation of such affects inadequate in themselves may give rise to a psychic trauma, provided there be sufficient coherency among the separate elements as regards their affective quality. One may conceive of the psychic trauma as acting in the manner of a foreign body, which, having gained entrance into the organism, is preserved there in unconscious association. That this conception is no mere figment, but that an invasion of the psychic organism by a hostile impression actually takes place, is proved from the fact that each morbid symptom straightway disappears as soon as the memory of the specific cause is fully awakened and is reacted to in a manner appropriate to the original affect. Breuer and Freud's thesis is then in first line to the effect that the hysterical suffers, for the most part, from *reminiscences*.

The striking phenomenon to be noted here is the extraordinarily vivid preservation in unconscious association of an event, perhaps so remote as to cover an interval of years, upon condition only that the emotional shock shall not have been commensurately reacted to at the time of its occurrence. With an adequate reaction the greater part of the affect is liberated, as in the familiar saying, "to have a *good cry*." If reaction is forestalled, its concomitant affect is, as it were, locked in, and the result of such congested affect is an emotional dead-lock. Hence, an unresented offence engenders feelings of "vexation," which are allayed only through the "catharsis" of an adequate retaliation. Similarly, one speaks of "making a clean breast of the matter," and the sense of relief following a thorough-going confession is a commonplace. Thus the spoken word may do duty for the overt act. This process of appropriate reaction whereby the affect is released is called *elimination* (Abreagiren). The painful affect, however, like the unsuited

pabulum of the ameba, may be disintegrated, as it were, through association with the remembered events occurring subsequently to the painful emotion, as in the event of fright the affect is assuaged in the remembrance of the incidents attending the rescue. This process analogous to the absorption of ingested material by the bodily tissues might fittingly be called *assimilation*.

To account for the inhibiting of the process of elimination, the authors cite the severity of the shock, the impediments of social conventions, and especially the nature of the occasion itself, which often entails a reminiscence which the patient wishes to evade, and which he therefore intentionally excludes from participation in current consciousness. The barriers to the process of assimilation are to be sought not in the content of the remembrances, but in the psychic condition in which the experiences out of which they arose were originally recorded. Thus, impressions quite innocent in themselves often owe their pathological significance to an accompanying emotional tension, *e. g.*, fright, or to such an abnormal psychic condition as is seen in the twilight states of day-dreams and allied conditions. So that it is the dissociated psychic state that renders impossible an adequate reaction through associative assimilation. Such dissociated states, in the opinion of Breuer and Freud, are present, at least in a rudimentary way, in every case of hysteria, and are a fundamental condition of the neurosis. In persons in whom such states occur there exists, therefore, a predisposition to hysteria. Given the emotional moment, the way is open for its manifestation in somatic effects—a mechanism to which Freud has given the name “conversion.”⁵ But even in individuals accounted normal, a sufficiently severe trauma, a painful repression, may induce such a dissociation of consciousness, and we then have the conditions of a psychically acquired hysteria.

So much for Freud's introductory work. From this time forward Freud studied the manifestations of unconscious⁶ processes in normal as well as in neurotic subjects. Each utterance of the unconscious became for him significant.⁷ In every trick of habit, every lapse of memory, every slip of the tongue or pen, in short, in every unpremeditated reaction of the individual, Freud read the significant expression of unconscious trends. In his rigid conception of psychical determinism no psychic manifestation may arise detached and isolated. But in accordance with the doctrine first posited by Leibnitz, Freud assumes the principle of psychic

⁵ Adolf Meyer has called this type of reaction a “substitution neurosis.”

⁶ For an appreciation of the significance of the unconscious as employed by Freud and as discriminated from the subconscious of Janet and of Prince, the reader is referred to the philosophical treatment of the subject in Bernard Hart's able paper, “The Conception of the Subconscious,” *Journal of Abnormal Psychology*, February-March, 1910.

⁷ Freud, *Zur Psychopathologie des Alltagslebens*, 3d ed., Karger, Berlin, 1910; *Der Witz und seine Beziehung zum Unbewussten*, Deuticke, Vienna, 1905; Maeder, *Contributions à la Psychopathologie de la vie quotidienne*, *Arch. de Psychologie*, t. vi, 21, 22, and t. vii, 27.

continuity as a necessary parallel to the law of continuity obtaining in the concomitant organic sphere. Every psychically conditioned reaction of the organism implies inevitable causal relations of direct significance in the life of the individual. In order to turn these intimations of the unconscious to scientific account, it behooves us to gain the key to their interpretation.

Out of this attempt important ramifications have arisen. Indeed, the outcome of this quest has been the development of the dynamic conceptions which represent the crux of Freud's psychology. Our psychic life is determined by affective states. Action is incited through purpose and predilection, and, in the absence of conscious social incentives, these are seen to be motivated in instincts which often enough disclose the imprint of their rude origin. To civilization belongs the task of evicting these unseemly trends through the substitution of higher, esthetic interests. It is precisely the conflict between these inherent lower trends and the ethical inhibitions of our sophisticated consciousness which prepares the ground for a neurosis. A neurosis, then, possesses an important social aspect. For it inevitably entails a discrepancy in the social relation. It is essentially a disaffection of the individual toward his social environment. Jung has said, "Every neurosis represents an individual attempt at the solution of a social problem." As social beings none of us is immune from the neurotic infection. In the attempt of civilization to eliminate from consciousness the unsavory vestiges of our psychic descent, we are all participants. But it is only when we subject these trends to undue strictures, and deny them share in contemporary consciousness, that there ensues the open rupture which we call a neurosis. This process of denying unwelcome elements entrance into consciousness, Freud has called the mechanism of *repression* (*Verdrängung*), a mechanism which constitutes the essential condition of the neurosis. The neurosis then presupposes the presence in the unconscious of suppressed psychic complexes, *i. e.*, systems of unconscious reminiscences which are painful and inadmissible because of their incompatibility with current social and ethical standards. Hence it is the task of the psychologist to bring the unconscious images of the patient into the high light of consciousness, that in the foreground of frank contemplation these ghosts of the unconscious may be divested of their terrors and rendered innocuous. To raise the boycott upon the unconscious is then the essential requisite. The philosopher Maeterlinck acutely divined the insidious power of the unconscious complex when he wrote that "an evil fate is as pliant in the fingers of wisdom as the blade of grass that one may cull, but in the hands of the unconscious it becomes as inflexible as a bar of iron."⁸ It is the enemy in ambush against whom we are powerless to cope.

⁸ Maeterlinck *La Sagesse et la Destinée*.

To bring into conscious view the images which are operating unconsciously, so that the patient may confront them openly and handle them intelligently, is then the basic aim of Freud's psychotherapy. This process of uncovering the complexes at the root of the neuroses has been called by Freud *psycho-analysis*. Broadly, the technique of the method is adapted to the purpose of liberating the patient's spontaneous associations. The details of the technique must vary with individual needs, to be determined only by the instinct of the physician. Because of the many modifications, therefore, to which the method is open, a comprehensive statement of its technique does not lend itself to exact formula. In the main, the technique as applied by Freud consists in having the patient, while resting in a recumbent position, give free expression to the thoughts arising spontaneously in his unreined fancy. Through this procedure it is seen in what channels the patient's mental images are wont to flow, what reminiscences are significant for him, what are his habitual preoccupations, his silent reservations, his suppressed trends, what, in short, are the psychic complexes⁹ determining his unconscious conflicts.

The latest word upon the technique of psycho-analysis was Freud's opening address at the Psycho-analytic Congress in Nuremberg in March. In discussing the resources of psychotherapy, he reiterated anew the central importance of directing the technique toward overcoming the patient's *resistances* (*Widerstände*). Therapeutically it is not the primary demand, he said, that we seek to ferret out severally, the patient's complexes but that we labor, above all, to efface the defensive inhibitions set by social conventions, and establish the complete *rapprochement* of patient and physician. With the attainment of a frank, unreserved attitude toward his physician (*Uebertragung*), the patient's complexes, having no longer warrant for their existence, are compelled *de facto* to capitulate, and the patient has closed the chapter of his neurosis.

Freud's technique has been valuably augmented by the association experiment of Jung.¹⁰ Through this procedure the physician becomes rapidly oriented with regard to the patient's dominant trends, and obtains a convenient survey of his general psychological reaction. In this simple procedure a series of test words are repeated to the patient, who is required to respond instantly to each with the first word that occurs to him. Having obtained the patient's average reaction time, a marked increase of this interval denotes that a complex has been aroused, the affective significance of which may be estimated relatively to the amount of the delayed reaction. Failure of reproduction or incorrect reproduction, that is, inability to recall the original reaction-word, on hearing the series of stimulus-

⁹ Jung, *Die Bedeutung des Vaters für das Schicksal des Einzelnen*, Deuticke, Vienna, 1909.

¹⁰ *Diagnostische Assoziationsstudien, Beiträge zur Experimentellen Psychopathologie*, Barth, Leipzig, 1906.

words repeated a second time, affords additional clue to an underlying complex. "Perseveration" affecting the succeeding reactions, repetition of the stimulus-word, mistaking it or failure to respond at all, are chief among the remaining complex-indicators. So that in the association experiment the physician is enabled to converse, as it were, with the patient's unconscious, and under strategic advantages which render any attempt at subterfuge wholly futile, every effort at evasion being circumvented by a resulting divergent reaction-time.

The chief resource, however, of both Freud and Jung, but yet the instrument requiring the greatest deftness of handling, is that of dream-analysis. This subtle method of obtaining insight into the processes of the unconscious has been developed in Freud's remarkable work, *Die Traumdeutung*.¹¹ This work is the *fiat lux* amid the nebulous chaos of dream-imagery. Through its genius the baffling, apparently incoherent congeries of dream-elements is resolved into form and significance, and rendered conformable to genetic principles. As the *Traumdeutung* represents the keynote of Freud's psychology, it is only through a mastery of this work that it is possible to obtain an adequate grasp of its author's conceptions. Obviously, it is impossible within the limits of the present paper to give more than a hint of its real import. Suffice it to say that the basic principle of dream-analysis, as posited by Freud, is the *wish-fulfilment*. In the phantasies which the unconscious conjures during sleep, life's frustrated quests come into their right. In the unchecked vagaries of sleep the primitive springs of action are released. Here are vented our coveted satisfactions, and our brute, primitive incentives. In the grotesque illusions of dream-creations, the unconscious slips its fetters and indulges its crude, archaic trends. However, one seeks in vain to discover the unconscious wishes in the patent, *manifest* content of the dream. It is only in the guise of veiled equivalents that the suppressed, expatriated trends of the unconscious venture to clothe their meaning—only in this *latent* content need we hope to divine the import of the dream. In its incredible cunning is entailed, perhaps, the most remarkable aptitude of the unconscious. It is in its distorted, artful forms of expression that we come upon the phenomenon of symbolization¹².

¹¹ Freud, *Die Traumdeutung*, 2d ed., Deuticke, Vienna. 1909; Ueber den Traum, Bergmann, Wiesbaden, 1907; Abraham, Traum und Mythos, Eine Studie zur Völkerpsychologie, Schriften zur angewandten Seelenkunde, Heft iv; Jung, L'Analyse des Rêves, L'Année Psychologique, t. xv; Maeder, Une voie nouvelle en Psychologie, Freud et son école, Casa Editrice del "Cœnobium," Lugano, 1909; Essai d'interprétations de quelques rêves, Archives de psychologie, t. vi, 24; Macfie Campbell, Psychological Mechanisms with Special Regard to Wish Fulfilments, State Hospitals Bulletin, N. Y., May, 1909; Ernest Jones, Freud's Theory of Dreams, American Journal of Psychology, April, 1910; S. Ferenczi, The Psychological Analysis of Dreams, American Journal of Psychology, April, 1910.

¹² Jung, Ueber Symbolik, Jahrbuch für Psychoanalytische und Psychopathologische Forschungen, 1910, vol. ii; Riklin, Wunscherfüllung und Symbolik in Märcen, Schriften zur angewandten Seelenkunde, Heft ii.

which constitutes the especial *métier* of unconscious mentation, for the unconscious delights in the cryptic and recondite.

An account of Freud's psycho-analytical method in the treatment of the neuroses, however brief, must not fail to include Jung's extension of the method into the domain of the psychoses.¹³ The arduous researches conducted by him at the Burghölzli Asylum in Zürich have vindicated conclusively the psycho-analytical method in psychiatry, for in applying the method in the study of insanity, it has been Jung's great service to open the way to the psychological interpretation of the psychoses. Through the method of psycho-analysis he appears to have established the psychological mechanisms upon which is based one of the most typical of the insanities, and in discovering the key to dementia præcox he has rendered animate and coherent many of the delusions, stereotypies, and obsessions before which clinical psychiatry has until recently stood baffled.

In the larger breadth, it has added to the vistas of genetic psychology, and in the importance of its theoretical implications, Jung's latest work in analyses of this type of regression is to be accounted among his most important researches.¹⁴ In this inquiry, conducted in detail by Honegger,¹⁵ a pupil of Jung's, a remarkable analogy appears to have been established between the apparently incoherent phantasies of a catatonic patient and the obsolete, metaphysical constructions of ancient mythology. In the naïve creations of fancy in which the patient seeks to formulate the universe there is reproduced the hypothesis of an earlier cosmogony. Hence, in entering through the method of psycho-analysis into the seemingly anomalous vagaries of this characteristic type of reversion, Jung believes that he has shown a correlation between individual and ethnical development in the psychological sphere analogous to that which obtains between the ontogenetic and the phylogenetic series in the sphere of biology. From the gist of this study we may infer something of the proportions to which psycho-analysis is destined to expand. It is seen that no narrow limits may be set to the directions of its application; that its value is not merely a therapeutic one, but that it is a method of investigation which offers promise throughout the range of mental science.

In America the application of psycho-analysis in the field of psychiatry has its able exponents in Adolph Meyer and August Hoch.¹⁶

¹³ Jung, *The Psychology of Dementia Præcox*, Journal of Nervous and Mental Disease Pub. Co., Monograph Series 3, 1908; *Der Inhalt der Psychose*, Schriften zur angewandten Seelenkunde, Heft iii.

¹⁴ Jung, *Ueber Symbolik*, op. cit.

¹⁵ *Ueber Paranoide Wahnbildung*, Jahrbuch für Psychoanalytische und Psychopathologische Forschungen, 1910, vol. ii. (Read in abstract at Psychoanalytic Congress in Nuremberg in March.)

¹⁶ *Psychological Bulletin*, 1907, iv, pp. 161 to 169.

Both Meyer¹⁷ and Hoch have long laid emphasis upon the psychological components of the psychoses, and have vigorously insisted upon the genetic point of view in psychiatry. Indeed, the psychogenic factors in the etiology of insanity have been for many years a favorite theme of Meyer's writings, "bad mental habits," "mis-carried instincts," "unhealthy trends," and "inadequate reactions" being among the dynamic determinants upon which he lays fundamental stress in his teaching.¹⁸ Perhaps, the chief difference between the conceptions of Freud and those of Meyer lies in the greater emphasis of the former upon the unconscious trends, while with Meyer the conscious factors tend to occupy a position nearer the centre of the field.

The insistence upon a broad biological point of view is an attitude common to both schools.

With regard to the attitude of the internists toward the psychic cases entering the medical clinics, Barker was among the first of the American clinicians to urge the study of the psychological factors in these conditions.¹⁹ In the cases treated by him at the Johns Hopkins Hospital he has adopted a technique which follows partly the method of psycho-analysis applied by Freud, the psycho-therapeutic aim being directed toward annulling the effect of the baneful impressions (psychic traumata) which have not been adequately reacted to, by permitting the elimination of the concomitant affect through verbal reaction.

In a recent article by Ernest Jones,²⁰ in which he pays a fitting tribute to the genius of Morton Prince, the writer calls attention to the fact that as early as nineteen years ago Prince recognized the therapeutic importance of propitiating a troublesome reminiscence by admitting it to consciousness and affording it the freedom of normal association through the channel of verbal reaction. It is interesting that in this position Prince has anticipated one of the most fundamental of Freud's conceptions—that of psychic elimination.

Prominent among the frank adherents of Freud's conceptions

¹⁷ An attempt at the Analysis of the Neurotic Constitution, *American Jour. of Psychiatry*, xiv; Fundamental Conceptions of Dementia Præcox, *British Medical Journal*, 1906.

¹⁸ An excellent résumé of Meyer's Conceptions is given in an article by Macfie Campbell: A Modern Conception of Dementia Præcox, with Five Illustrated Cases, *Rev. of Neurology and Psychiatry*, October, 1909.

¹⁹ Barker, *The Psychic Side of Medicine*, 1907, *The University Record* (Chicago) xii, 12 to 18; On the Psychic Treatment of Some of the Functional Neuroses, 1907, *Internat'l Clinics*, 17th series, vol. i, 1 to 22; On Neurological and Psychiatric Diagnosis, 1907, *Transactions of the Congress of American Physicians and Surgeons*, vii, 9 to 16; Some Experiences with the Simpler Methods of Psychotherapy and Reëducation, 1906, *American Journal of the Medical Sciences*, October; Introduction to the Study of the Nervous System, 1910, *Osler's Modern Medicine*, vol. vii.

²⁰ Bericht über die neuere englische und amerikanische Literatur zur klinischen Psychologie und Psychopathologie-Jahrbuch für Psychoanalytische und Psychopathologische Forschungen, Band ii, 1 Hälfte.

in America are Putnam,²¹ Jones,²² and Brill.²³ These authors have contributed ably toward the vindication of Freud's views. Through the study of his psychology and the application of the psychoanalytic method in the treatment of their patients, they have corroborated fully the psychological principles established by him.

Of the experimental psychologists, G. Stanley Hall has been foremost in the acclamation of the psychological methods advocated by Freud in the treatment of the neuroses. In his classic work, *Adolescence*, he was the first to give due recognition to the psychopathic researches upon which Freud had then but recently entered. It is hoped that this brief attempt to indicate the ascendant tendency of psychopathology to place psychic disorders upon a rational, scientific basis through the study of the mechanisms underlying them may incite a wider interest in the psychology of these processes. Psychotherapy has not lacked for adventitious aids, which undoubtedly have their place; but being merely adjuncts and irrelevant to the inherent situation, such agencies are necessarily restricted and inadequate. There is need of a more thorough and consistent study of the psychology of the neuroses with a view to determining the essential causative factors in the production of these processes, and to discovering cognate principles under which observed phenomena may be resumed. In the absence of an appreciation of the mechanisms involved in the morbid regressions presented in the neuroses, as interpreted by Freud and Jung, psychopathology is seriously hampered. There is a psychology of "nervousness," and a knowledge of its principles is the requisite equipment for an adequate understanding of neurotic conditions.

²¹ Personal Impressions of Sigmund Freud and His Work, with Special Reference to his recent lectures at Clark University, *Journal of Abnormal Psychology*, vol. iv, No. 5; The Relation of Character Formation to Psychotherapy, Symposium of Psychotherapeutics, *Journal of Abnormal Psychology*.

²² Psycho-analysis in Psychotherapy, Symposium of Psychotherapeutics, *Journal of Abnormal Psychology*; The Oedipus-Complex as an Explanation of Hamlet's Mystery; *American Journal of Psychology*, xxi; On the Nightmare, *American Journal of Insanity*, January, 1910, vol. lxvi, No. 3.

²³ Freud's Conceptions of the Psychoneuroses, *Medical Record*, December 25, 1909; Freud's Selected Papers on Hysteria and other Psychoneuroses, *Journal of Nervous and Mental Disease Publishing Co.*, Monograph Series, No. 4, 1909; Psychological Factors in Dementia Præcox, *Journal of Abnormal Psychology*, vol. iii, No. 4; A Case of Schizophrenia, *American Journal of Insanity*, vol. lxvi, No. 1.

FLUOROSCOPY OF THE GASTRO-INTESTINAL TRACT.

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FLUOROSCOPY was one of the earliest practical applications of the x -rays. However, the value of permanent radiographs in surgical diagnosis, together with a large number of burns of patients and operators in the early fluoroscopic examinations, has been responsible for sufficient adverse criticism to dampen fluoroscopic enthusiasm. The pioneer x -ray operators in Europe and America bear permanent scars that testify to the dangers of unprotected fluoroscopy, but the knowledge regarding the irritative possibilities that has been gained through calamities to pioneer Röntgenologists will serve to dispel this fear and establish fluoroscopy in the widening horizon. When we look upon the martyrs of Röntgenology we become reassured, for it is only the pre-protection period Röntgenologist or careless experimenter who has furnished us object-lessons. We have yet to note injurious x -ray effects upon the Röntgenologist who has worked with lead screen and protected tubes. We cannot, up to the present day, estimate the ultimate effect of the hard, penetrating portion of the radiations from an x -ray tube. We do know the results of continuous or interrupted exposure to the soft rays, and are able to guard against them. In no new departure of medicine and surgery have there been so many to enter upon its pursuit with such meager knowledge of its possibilities and dangers. This not only resulted in harm to these neophytes, but has also acted as a hindrance to the propagation of exact Röntgen knowledge. There has been, and probably still is, much x -ray work which is carried on with carelessness and ignorance. The scientific application of the x -rays suffers accordingly. The suggestion is then in order that such legislative action be taken as may preclude the use of the x -rays in other than skilled hands. This would mean elimination of the manufacturer, electrician, photographer, and others without medical training from a field where only exact knowledge and careful application will eliminate ill-effects.

The gigantic possibilities of fluoroscopy make it important for us to pursue its study only with such protected apparatus that no ill-effects may ever be reported. Constant use of and familiarity with fluoroscopic technique may lead one to a carelessness against which the Röntgenologist must conscientiously labor. This admonition is likewise applicable to all manner of x -ray application.

A review of the fluoroscopic situation indicates that the American has attempted to promote radiographic technique that would obtain the diagnostic information upon a succession of negatives

which the fluoroscope reveals at a glance. There is only one radiographic technique up to the present time that can approach ordinary fluoroscopy; we refer to the Bio-röntgenography of Rosenthal, Rieder, and Kaestle, that Röntgen triumvirate of Munich. The expense of this latter method places it without the realm of practical usefulness.

While the American has been venturing his rapid radiography, the European of France and Germany has been perfecting a fluoroscopic technique that avoids by ample protection the inherent dangers peculiar to the x -rays. The original fluoroscopic device of the Guilleminot type, with inefficient protection, followed by the cumbersome protected apparatus of the Albers-Schoenberg type, are giving way to the convenient Bécélère type. The new Dessauer kliniscop has some advantages over the Bécélère. These latter types of fluoroscopic apparatus have the tube in an amply protected, freely movable, x -ray- and light-proof box, the adjustments of which permit all manipulations of tube and diaphragm by one hand. The lead-glass covered fluorescent screen is adjustable, allowing the patient to be placed either sitting or standing between the screen and the tube box. The Dessauer kliniscop has the advantage of permitting examinations in the recumbent position also, similar to the trockoskop of Haenisch or Holz knecht.

The advantages of fluoroscopy cannot be gainsaid. Radiographic substitutes cannot, in any succession of radiographs, give the diagnostic information that the fluoroscope supplies, without the expense and tedious process of negative development. The inexpensiveness and immediate usefulness of fluoroscopic facts are incontrovertible arguments. The possible dangers can be guarded against by proper protection of patient and operator.

The peculiar superiority of fluoroscopy over radiography depends in the ability to study the peristalsis and surgical anatomy of the alimentary tract. We may study the physiological or pathological conditions which influence the position and relations of the esophagus, stomach, and intestines, with reference to the adjacent organs and bony skeleton; the anchorage of stomach and intestines, either normal or influenced by adhesions; the disposal of food in the gastro-intestinal tract; pathological filling defects and abnormalities of contour as presented by alterations in the tissues or interference with muscular function of the gastro-intestinal tract.

The fluoroscopy of the gastro-intestinal tract requires modern protected apparatus. It must be used in a totally dark room that will permit the inspection of the leaded glass fluorescent screen without shading the screen. The bellows type of fluoroscope is not useful in the least; it leads to incorrect estimates of shadow values and is woefully inexact. It would be splendid if the bellows fluoroscope were eliminated entirely. It is responsible for so many

ill-effects and adverse criticisms that we would delight in a bonfire of those now on earth and ostracise the manufacturer of any duplicates.

The author's technique of fluoroscopy consists in the use of the Bécélère type of apparatus in a totally dark room. The current to the tube is controlled by a floor switch in the primary circuit, which is opened or closed by the foot of the operator. The tube is regulated by a weighted string which operates an adjustment upon the regulating bulb of the tube and is at the right hand of the operator. With the water-cooled tube, regulation is seldom required. We employ a continuous current of water in the tube, after a fashion seen at the Albers-Schoenberg-Haenisch Institute at Hamburg. This consists of a 2-gallon bottle, with a small rubber tubing attached to an outlet in lower segment. This bottle is placed about two feet above the tube. After circulating in the water-cooling compartment of the tube, the water runs off through a second tube to a container upon the floor.

Into the frame of the lead-glass covered fluorescent screen is fitted with thumb screws a piece of plain glass, upon which may be charted the outlines of the bismuth-filled organs and the anatomical landmarks, with blue and red fat-pencils. These charting glasses are readily changed and their markings may be copied later upon thin paper for record. It is poor policy to chart upon the lead-glass of the fluorescent screen, as one will not have time to copy and erase the sketches.

The patient is prepared for the examination by a fast of four to six hours; the removal of the clothing to the hips; metallic markers are placed upon the ensiform and umbilicus; the patient may either stand erect or sit upon a movable bicycle seat, between the movable tube box and the screen.

For the examination there are required bismuth capsules of varying sizes; paste of bismuth, sugar of milk, and water; bismuth in water, and bismuth porridge. We use a fairly thick porridge of cream of wheat, into which 40 to 60 grams of bismuth oxychloride or carbonate is thoroughly mixed. This is the established Riederische Mahlzeit, when flavored with raspberry syrup. We prepare this in a chafing dish at the office or in the kitchen at the hospital.

The scheme of Holzknécht for gastro-intestinal fluoroscopy, as outlined in his monograph¹ may be simplified as follows: The patient is placed in the right anterior oblique position, and offered the small bismuth capsule. When the current is applied he is instructed to swallow. The route and rate of the capsule in the esophagus is noted until it reaches and passes through the cardiac orifice of the stomach. The succeeding larger types of the capsules are then offered and their course noted. By this means we are able to determine the location and lumen of an esophageal stricture. The

capsules do not always find the orifice of a diverticulum; therefore we employ the bismuth paste, about a level teaspoonful of bismuth carbonate and sac. lac., half and half. This is swallowed at the suggestion of the operator and after the x -ray is turned on. The use of bismuth and water (2 drams of bismuth to 2 or 3 ounces of water) is then employed. By carefully noting the passage of the paste and the water mixture one can determine the pressure of esophageal strictures, diverticula, abnormalities due to adhesions, cardiospasm, dilatations, pleuritic tugs, esophageobronchial fistulæ, carcinomatous filling defects and alterations of outline, pressure of aneurysms or tumors upon the esophagus. The description of the fluoroscopic symptomatology of each of these conditions is worthy of a distinct and separate descriptive paper.

Personally, we feel that the role of fluoroscopy in gastric diagnosis is most alluring and satisfying. While certain diagnostic phenomena may be obtained from the inspection of a mixture of bismuth and water immediately after its ingestion, one should depend rather upon the Riederische Mahlzeit immediately following its ingestion. The phenomena of interest brought out by the water and bismuth are, briefly, as follows: The disposition of the mixture by the stomach—whether it immediately reaches the caudal pole and pylorus; if it does reach the pylorus, does some of it enter the duodenum before the reflex closure of the pylorus is provoked by the ingestion of food into the stomach. Upon this point rests the estimation of a patulous pylorus. Because the bismuth and water does not enter the duodenum at once, one should not assume that there is a stenosis of the pylorus, as the pyloric reflex may have been occasioned by the esophageal reflex.

Succeeding the fluoroscopy of the esophagus and stomach by these simple measures we instruct the patient to eat slowly the ten or twelve ounces of bismuth porridge. This may take some time, as we frequently find gastric patients unused to such food.

To simplify and curtail this paper, we shall list the fluoroscopic symptoms of the more common gastric conditions in which this method offers such valuable diagnostic assistance:

FLUOROSCOPIC SYMPTOMS.

I. PYLORIC STENOSIS. (1) Dilatation of the stomach, both longitudinally and transversely. (2) Antiperistaltic waves running from the pylorus to the greater curvature. (3) Interference with the emptying of the stomach, the exit of the food being delayed eighteen to forty-eight hours; Suspicious symptoms which should be noted are: More or less degree of distention of the stomach; weakened peristalsis; food delayed in exit twelve to twenty-four hours; adhe-

sions of the pyloric area, which produce a fixed pylorus; pyloric filling defects; absence of any peristalsis at the pylorus, the wave running only from the greater curvature to the prepyloric area. The pyloric stenosis, whether produced by infiltrations and cicatrices about an ulcer or carcinoma, would produce almost identical symptoms. The differentiation can be determined by the stomach analysis, case history, and subjective symptoms.

II. GASTRIC CARCINOMA. Gastric carcinoma presents the following fluoroscopic findings: (1) Irregular filling defects in the outline of the stomach wall. (2) Abnormal peristalsis, there being no waves at the site of the filling defect; or, if the carcinoma involves the pylorus, antiperistaltic waves are seen. (3) Hourglass contraction where there is involvement of the middle portion of the stomach. The bismuth meal or water may be seen trickling through the narrowed lumen. (4) Adhesions of the stomach to adjacent organs, due to perigastric inflammation. (5) The lumen of the stomach is usually much smaller than normal, excepting, when the carcinoma involves the pylorus, we may have a dilatation.

III. GASTRIC ULCER. (1) Filling defects, which are not as irregular in outline as in carcinoma, the filling defect being due more to an irritation of the muscular action than to irregular outlines of mass changes in the stomach wall. This interference with the peristalsis in ulcers of the lesser or greater curvature is interesting. Where the ulcer involves the pylorus we have the additional symptoms previously noted when there is interference with the exit of the food.

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The author has selected the preceding references from a large number of books, monographs, and papers, as embodying the classical features of gastro-intestinal fluoroscopy.

REVIEWS.

AMERICAN PRACTICE OF SURGERY. Edited by JOSEPH D. BRYANT, M.D., LL.D., and ALBERT BUCK, M.D., of New York City. Complete in eight volumes. Volume VII. Pp. 961, with 396 illustrations and 7 colored plates. New York: William Wood & Co., 1910.

THE seventh volume of the *System of Surgery*, edited by Drs. Bryant and Buck continues the discussion of regional surgery as follows: Surgical diseases and wounds of the pelvic and gluteal regions, by Dr. Chas. H. Peck, of New York City; surgical diseases of the extremities, by Drs. C. A. Porter, and W. C. Quimby, of Boston; of the abdominal wall, by Dr. J. D. Griffith, of Kansas City; diagnosis of abdominal tumors, by Dr. M. S. Harris, of Chicago; abdominal section, by Dr. Wm. McD. Mastin, of Mobile; vascular surgery, by Drs. Le Conte and F. T. Stewart, of Philadelphia; surgery of the stomach and œsophagus, by Dr. A. J. Ochsner, of Chicago; surgery of the diaphragm and subphrenic abscess, by Dr. J. C. Reeve, of Dayton, Ohio; surgical treatment of peritonitis, by Dr. A. J. McCosh, of New York City; tuberculous peritonitis, by Dr. N. Jacobson, of Syracuse; abdominal hernia, by Dr. E. W. Andrews, of Chicago; surgery of the vermiform appendix, by Dr. A. J. McCosh; of the intestine, omentum, and mesentery, by Dr. Chas. W. Oviatt, of Oshkosh, Wisconsin; and surgical diseases of the anus and rectum, by Dr. J. P. Tuttle, of New York, and Dr. Samuel T. Earle, of Baltimore.

These various articles maintain a fair standard of excellence, and show that in most instances the editors have chosen the authors with discretion. Dr. Peck makes the most of a department of surgery apt to be slighted. His discussions of sacro-iliac disease, of sciatica, and of pilonidal sinuses are particularly noteworthy. Drs. Porter and Quimby have not been so successful in their discussion of the miscellaneous affections included with the surgery of the extremities; there is no classification, and many of the topics might better have been discussed in earlier volumes where they properly belong.

The monograph by Le Conte and Stewart, occupying nearly 200 pages, is a carefully prepared and accurate exposition of the modern surgery of the vascular system, and will take its place beside that

of Matas (in Keen's *Surgery*), recently reviewed in these columns. While the experience of Matas has been vast in all departments of vascular surgery, there are few if any surgeons, in this country at least, who have had as much experience, and enjoyed such success, with wounds of the heart, as has Dr. Stewart. Apart from the practical value of this monograph, considerable historical matter is included, and the entire composition is marred only by the insufficiency of the references to original sources of information.

The series of monographs on abdominal surgery is of unusual excellence, and though there is a certain amount of intrinsic evidence that the authors completed their work one or two years before the publication of the volume, the articles are nevertheless very satisfactory expositions of the science and art of abdominal surgery. Dr. Mastin (whose contribution, as well as those of Drs. Griffith and Harris, is separated from the abdominal section of the work by the section on vascular surgery) does well to emphasize the importance of making a diagnosis before opening the abdomen; it sometimes seems as if the more proficient a surgeon becomes in abdominal technique, the less careful he is to reach a reasonable accurate diagnosis before "taking off the lid." Dr. Ochsner recommends immediate operation for gastric perforation only during the first twelve hours after the accident; he advises a *long* abdominal incision, and practises gastric lavage *during* the operation and before suture of the perforation. In the case of patients coming under the surgeon's care at a later period than twelve hours, he thinks each case should be judged on its merits; and that where there is a probability of the closure of the perforation by a plug of omentum it may be wise to sustain the patient with exclusive rectal feeding until an abscess forms, which abscess may then be drained. This teaching is in accord with the same surgeon's views as to operation for appendicitis; and if only other surgeons did not misunderstand the teaching, and believe that it is possible by "Ochsner's method" to cure such patients without operation, many lives would be saved. The important point is that operation is required sooner or later in all patients who do not die while the diffuse peritonitis is subsiding; and it is with considerable surprise that we find that McCosh, whose untimely death in 1908 will long be regretted, states that a delay of a day or two may often be an advantage after a residual abscess has formed, in allowing the general peritoneum to be more securely walled off from the localized process. This we hold to be an erroneous view; unless the abscess which forms as peritonitis subsides under the "Ochsner treatment" is opened very soon, it may leak through its adhesions, causing a secondary diffuse peritonitis from which the patient will not recover under any form of treatment. In few cases is delay so dangerous.

McCosh's views on appendicitis, though radical, we believe to be more truly conservative of life than those of surgeons who are

willing to temporize with a most treacherous disease. He says: "There is no surgeon living who can *know* that an ulceration is not rapidly approaching the serous coat of the organ," and he urges immediate operation in every early case; in cases with diffuse peritonitis he urges immediate operation except in patients past middle life with bad livers or kidneys (in such patients he thinks the Ochsner treatment preferable); and immediate operation is also advised in cases of abscess, but he reiterates his belief that if the abscess has formed as a diffuse peritonitis subsides, a delay of a few hours or days may be beneficial.

Dr. Ochsner's reference to the benefit to be derived from drainage of the stomach by gastro-enterostomy at its lowest point seems an indication that these paragraphs were penned some years ago; since there is at present quite sufficient evidence that gastro-enterostomy is not a drainage operation except when the pylorus is obstructed, and that even under such circumstances the location of the opening at the lowest point of the stomach is of no advantage so far as drainage is concerned.

Reeve's article also is scarcely up to date; he apparently is unfamiliar with Barnard's admirable lectures on subphrenic abscess (1908); and we have read Oviatt's chapter on the intestines without finding even a mention of congenital megacolon, the so-called Hirschsprung's disease. This whole article is very sketchy, reading like a student's quiz compend, and being notably weak in pathology, and giving no idea whatever of prognosis.

The illustrations throughout the volume are scarcely up to the standard of those in other modern works; conspicuously poor are the smears of printer's ink furnished as illustrations of the anatomy of hernia. Plate 100 precedes a series numbered 48 to 52; the legend to Plate 52 faces Plate 51, and Fig. 21 is upside down.

A. P. C. A.

DIE SYPHILIS DER NASE, DES HALSES, UND DES OHRES (SYPHILIS OF THE NOSE, THE THROAT, AND THE EAR). By DR. P. H. GERBER, Professor in the University, and Director of the Royal University Policlinic for Throat and Nose Patients at Königsberg. Second edition; pp. 144, with four colored plates. Berlin: S. Karger, 1910.

THIS volume is more than a second edition of the first, of which, to quote the author's preface, hardly one stone remains upon another. It is a condensed and in some measure statistic summary of the facts developed from the records of syphilis of the throat, nose, and ear reported in general, with a bibliography of sixteen octavo pages. The great significance in syphilitic lesions in the

mucous membrane of the upper air passages is declared to depend upon three conditions: (1) The occasionally relatively early appearance of subjective difficulties and functional disturbances and their chronic progress; (2) the production of a copious secretion which threatens easy extension of the disease; and (3) the great tendency to destruction shown by the syphilitic products, and which penetrate into the adjoining cartilaginous and osseous tissues. Then there are the destructive processes at the orifices of the respiratory and digestive tracts which leave lifelong stigmata—destructive processes that sometimes directly endanger life.

In the author's practice 672 cases of syphilis of the upper air passages were noted in 73,663 patients, of which 4 were primary, 105 secondary, and 329 tertiary. The nose was the seat of lesion in 231 cases, the rhinopharynx in 59, the mouth and pharynx in 481, the larynx and trachea in 115, and the ear in 33. Of the whole 672, 231 had tertiary nasal syphilis.

The lesions occurring in each division of the subject are detailed; in some instances accompanied by brief records of exemplific cases. A series of four plates at the close of the volume contain excellent colored representations of a few of the conditions described in the text.

J. S. S.

GENERAL BACTERIOLOGY. By WILLIAM DODGE FROST, Associate Professor of Bacteriology in the University of Wisconsin, and EUGENE FRANKLIN McCAMPBELL, Professor of Bacteriology in the Ohio State University. Pp. 332; 61 illustrations. New York: The MacMillan Company, 1910.

THIS book is extremely comprehensive in its scope, aiming at no less than a survey of the whole subject of bacteriology. Naturally, limitation of space has rendered detailed treatment of the various divisions impossible. Still, conciseness of expression and an excellent sense of proportion have enabled the authors to compress a large amount of information into small compass. Beginning with a brief sketch of the history of the subject one is carried logically through the morphology of bacteria, the methods used in their study, the principles and methods of classification, and the physiology, metabolism and relation of bacteria to environment. The biology of the specialized groups of bacteria is next considered, 50 pages being devoted to the pathogenic organisms. Under the Distribution of Bacteria there are chapters on bacteria of the soil, of the air, of water and sewage, of milk and its products, and of the human body.

The book is not a thesaurus for the sake of reference use, nor is it a compend of practical points for the worker in this field. It is

purely educational, regarding bacteriology as a branch of biology, and may be commended to the student for use in conjunction with laboratory work and more specialized manuals in order to give him a perspective in his work and the rationale of various methods. To those specializing in this field the book is of interest as affording in brief space a broad view of the whole subject. Feeling that this has been the intent of the authors and that they have acquitted themselves very creditably of a difficult task it would be unfair to mention in a critical way the shortcomings of the chapters which are of especial interest from the standpoint of medicine such as incompleteness of the list of pathogenic bacteria and inadequate descriptions. There are many books which cover these omissions. When perused for its general educational value there is no one who is interested in any aspect of bacteriology who will not obtain much that is interesting and of value.

D. B. P.

A TREATISE ON DISEASES OF THE SKIN. FOR THE USE OF ADVANCED STUDENTS AND PRACTITIONERS. By HENRY W. STELWAGON, M.D., Ph.D., Professor of Dermatology, Jefferson Medical College, Philadelphia. Sixth edition, revised. Handsome octavo of 1195 pages, with 289 text illustrations, and 34 full-page colored and half-tone plates. Philadelphia and London: W. B. Saunders Company, 1910.

THIS new edition of Stelwagon's well-known and deservedly esteemed *Treatise on Diseases of the Skin* shows evidences of careful, painstaking revision in almost every section, the section on pellagra, a disease which has rather suddenly assumed great importance recently in the United States, having been entirely rewritten. The author is not inclined to accept the long-prevalent theory that this malady is due to the eating of spoiled maize, but thinks it more likely that it is caused by some protozoön, a view which just now seems to be gaining an increasing number of supporters. A number of tropical affections are included in this edition for the first time, among them that extremely mutilating disease gangosa, which we have acquired, along with numerous other undesirable things, with our colonial possessions in the East. Sporotrichosis, a comparatively recent addition to the already long and rapidly growing list of cutaneous infections, is likewise treated for the first time.

The so-called grain itch is thought by the author to be, in many cases at least, identical with the pruritic disease known as "prairie itch," an annoying affection which has been prevalent off and on for years past in a number of the Western States. There is apparently but little doubt that these two affections are one and the

same, both being due to the *Pediculoides ventricosus*, whose causal relationship to grain itch has only quite recently been discovered.

The chief therapeutic novelty which finds mention in this edition is the so-called carbon dioxide snow, introduced into dermatological therapeutics by Pusey. The author gives with some detail directions for the use of this very manageable and, in properly selected cases, efficient caustic. The very great value of this agent in the treatment of vascular nævi and certain other newgrowths of the skin was immediately recognized upon its introduction, and its use has grown very rapidly.

The many admirable illustrations which it contains have always been one of the most valuable and attractive features of the book, illustrating the text in the most effective manner. Twenty-five new ones have been added to this edition, while a few of the older and less satisfactory have been omitted.

These additions and revisions, incorporating the most recent acquisitions to our knowledge of diseases of the skin, bring the book fully up to date, and it continues to be what it has been from its first appearance, one of the best treatises on the subject.

M. B. H.

THE RELIGIO-MEDICAL MASQUERADE. By FREDERICK W. PEABODY, LL.B. Pp. 197. The Hancock Press, Boston, 1910.

THIS contribution, in a very bitter tone, to the controversial literature of "Christian Science" is interesting as coming from a lawyer of standing, who has been engaged in several suits involving Mrs. Eddy and other various members of her sect, and thus made acquaintance with vast amounts of sworn testimony and read many unpublished letters. His conclusions are uncompromisingly stated, and he refuses to be ranked with the weak-minded who think "there must be something in it." He asserts the inventor to be "mercenary, insincere, shameless, and bold to a degree surpassing that of all other persons who have duped mankind. Upon theft and falsehood she has laid the foundations of the 'religion' by which she has accumulated a fortune." He is not content with assertions; he quotes chapter and verse, as in the accounts of the death of Mrs. Eddy's coachman, who expired (in her house) of a disease of which he had been "completely cured," and of the end of her English "show convert," the Earl of Dunmore. The latter had been "healed" after being told by an eminent London surgeon that his disorder was incurable. So he sat on the platform and testified and wrote articles, etc.—the only misfortune in the case being his death of the very disease of which he had been cured. Mr. Peabody's final conclusion is that except the honestly deluded, the whole lot are "in a skin-game" together.

J. K. M.

INDUCED CELL REPRODUCTION AND CANCER. By HUGH CAMPBELL ROSS, M.R.C.S., L.R.C.P., Director of Special Researches at the Royal Southern Hospital, Liverpool. Pp. 423; 129 illustrations. Philadelphia: P. Blakiston's Son & Co.

THIS widely heralded book, after an introductory preface of distinct interest as to how the author's method of research came to be developed, presents the subject in seventeen chapters and four appendices. The studies by the author and his collaborators have been made especially on human leukocytes, the cells being placed on a 1 per cent. agar film and covered with a cover-slip. The stains and the various chemical substances are dissolved in the agar solution and act upon the cells by diffusion into them after the preparation has been made. Records of the various changes observed are made upon photographic plates by a very ingenious photomicrographic apparatus devised by the author. An interesting algebraic formula for the mixture of the agents that are to act on the cell has been elaborated and depends on predetermined "units" which by multiplication and addition equal the "coefficient of diffusion" of the particular type of cell in question. Some interesting early conclusions indicate that the blood platelets are living cells, and that basic degeneration of the erythrocytes is due to breaking up of the nucleus. Following this it was noted that alkaloids in the agar jelly excited what is called increased amoebic activity, the most active being atropine. The next important observation was that extract of prevertebral lymph nodes of sheep excites division in the lymphocytes, and the statement is made that "the nucleus does not vanish; it forms the spindle. The chromosomes are not derived from within the nucleus, but are formed from the normal Altmann's granules which exist in the cytoplasm. The centrosomes are not mere 'dots' at the poles of the spindle, but are derived from the nucleolus, which has divided into two." The further statement is made that the chromosomes may number 8, 16, 32, or some number between these figures, and that the more rapid the division the fewer the chromosomes. Asymmetrical division and division into several daughter cells is described as very common. Furthermore, the chromosomes may split either longitudinally or transversely. Division could be induced only in cells on the jelly not in cells suspended in a solution containing the same agents. After some experimentation similar changes were produced in polymorphonuclear leukocytes, and the startling discovery made that the so-called lobes of the nucleus are really centrosomes. Other "auxetics" (exciters of reproduction) were found in the azur constituent of polychrome methylene blue, and in some elements in putrefied adrenal extract, believed to be similar to kreatin, xanthin, globin, or probably to some of the amido-acids. The auxetic action of globin is shown in the successful treatment of chronic leg ulcers

by means of its application, but always with intervening suppuration. From this the author argues that some similar auxetics must account for the proliferation of cancer cells, the ultimate cause thus being destruction of tissue with resultant excessive atypical multiplication. Such proliferation normally is inhibited by a demonstrable inhibitory action of normal serum. Treatment, therefore, was instituted in two cases of cancer by rectal injections of defibrinated sheep's blood with apparent improvement of the patient's general condition.

The reviewer cannot attempt to analyze all the points made in the book, but would say that the statements in regard to cell division, which are fundamental in the argument presented by the author, are dogmatic and lack convincing proof either in the text or in the pictures. The author ignores many well-founded observations on living protozoa and shows little knowledge of many important biological facts. Questionable statements in regard to pathological problems are made, such as: "The phenomenon of healing is due to the proliferation of white blood cells which multiply by cell division to repair the tissues which are damaged" (page 168); "mutation—an acquired characteristic suddenly becoming hereditary for all succeeding generations" (page 369). He uses curious terms for well-known parasites, *e. g.*, "trypanema pallida," "trypanosomes amœbæ (the causes of dysentery)." Errors of this kind tend to limit confidence in the accuracy of other statements made and seriously hamper the logic of the argument in the mind of a critical reader.

Professor Harvey Gibson and others have written open letters to the *Lancet* (December 31, 1910) in reference to the appearance of their names in the book, and the author has answered them in a letter to the same magazine (January 4, 1911). This correspondence is of such a personal nature, however, that it should be given no great weight in a purely scientific estimate of the worth of the author's researches.

Mechanically the book is well made up; it is printed in large clear type, on heavy white paper and profusely illustrated, the illustrations being well correlated with the text. The subject matter is presented clearly and in logical sequence, and should be intelligible to even the lay reader, but to the scientific reader it lacks the conciseness which a more liberal use of technical terms would insure; and in many places frequent repetition of previously stated observations and detailed explanations of points well understood by the tyro in biological science render the book tiresome and verbose.

H. T. K.

DISEASES OF THE COLON AND THEIR SURGICAL TREATMENT. By P. LOCKHART MUMMERY, F.R.C.S. (Eng.), B.A., M.B., B.C. Cantab., Jacksonian Prizeman and Late Hunterian Professor, Royal College of Surgeons. Pp. 322; 88 illustrations. New York: William Wood & Co., 1910.

THIS book, the preface tells us, "is founded upon the essay which was awarded the Jacksonian Prize for 1909 by the Royal College of Surgeons." Opening with an account of the anatomy and development of the colon, there follow chapters on the physiology, morbid physiology, and bacteriology of the colon, with a consideration of methods of diagnosis. The chief diseases of the colon for which surgical treatment may be required are then discussed at the length of a chapter each, including such subjects as congenital abnormalities, volvulus, adhesions and kinking, enteroptosis, intussusception, chronic mucous or membranous colitis, ulcerative colitis, pericolitis, tuberculosis of the colon, chronic constipation and fecal impaction, simple stricture of the colon, embolism of the mesocolic vessels, simple tumors of the colon, malignant disease of the colon, and traumatism; while the volume concludes with a brief description of the various operations which have been recommended in earlier portions of the work (colotomy, appendicostomy, resection and anastomosis of the colon). The surgery of the rectum is not included.

While the entire work is distinctly Anglican in conception and execution, only the most casual acquaintance being exhibited with the work of surgeons on the Continent of Europe and in this country, the volume, nevertheless, is a welcome addition to the rather scanty literature of a subject which is yearly coming to occupy a larger portion of both surgical thought and practice. Among the most interesting chapters are those dealing with chronic forms of colitis. Mummery objects to the terms mucous and membranous colitis as indicating a symptom-complex which may be due to various pathological states; he thinks "chronic colitis" a suitable name, provided the one using it admits the disease under discussion to be really a chronic inflammation of the colon and not merely a neurosis; and he presents figures which tend to show that there is nearly in every case a definite pathological change in the colon sufficient to account for the symptoms. He speaks enthusiastically of appendicostomy as the ideal remedy for patients whom medical treatment has failed to relieve; and from his personal experience in five cases, evidently is a competent judge.

In speaking of strictures of the colon, as also of the rectum, which still are regarded by many surgeons as due to tertiary syphilis, he states that after a careful search he has "not succeeded in finding a single instance of an undoubted syphilitic lesion, much less of a syphilitic stricture." The figures he presents of operations for

malignant disease with acute obstruction, supervening on chronic, merely serve to emphasize the danger of radical operation and the comparative safety of the two-stage procedure.

The volume will prove more useful for reference if in a second issue it shall be more carefully edited, that is, the subject matter rearranged, condensed, and systematized.

A. P. C. A.

THE EAR AND ITS DISEASES. By ALBERT A. GRAY, M.D., Laureate of the Lenval Prize in Otology, International Medical Congress, 1909; Surgeon for Diseases of the Ear, Victoria Infirmary, Glasgow. Pp. 388; 123 illustrations. New York: Wm. Wood & Co., 1910.

As one new feature, the back cover of this volume contains a sheath enfolding a strip of set lenses for due study of its thirty-seven stereoscopic photographic illustrations. Another valuable feature consists of sixteen initial preliminary pages on acoustics for better appreciation of the physics involved in the production and sensation of sound. These are exceptionally excellent. Then follow chapters on anatomy and physiology, methods and principles of investigation, general semeiology and therapeutics, the relationship of nasal and pharyngeal affections to diseases of the ear, and on the injuries and diseases of the outer ear; concluding with several pages on deaf-mutism, and a few paragraphs as to the bearing of ear disease upon life insurance. All these subjects are duly illustrated, largely with photographs and photomicrographs of normal and pathological specimens prepared and photographed by the author.

The text is terse and comprehensive; the teaching good, and indicative of practical experience. Little attention is accorded to theory or procedure of doubtful import, while well-known and well proved measures are not unduly elaborated. Caution is counseled in instituting radical surgical measures on the one hand, and very few surgical instruments and appliances are figured on the other. As a supplementary volume, instructive on a number of useful points untouched in the ordinary text-book, it is well worth a place in the library of the working otologist.

J. S. C.

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF
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On the Acquisition of Tolerance to Salvarsan by *Treponema Pallidum*.
—GAUCHER and GUGGENHEIM (*Bull. et mém. Soc. méd. d. hôp. de Paris*. 1911, xiii, 174) have made a careful clinical study of cases of lues treated with "606," which would tend to throw light on the alleged power of *treponema pallidum* to acquire arsenic resisting properties such as Ehrlich found for trypanosomes. In considering some cases treated originally with hectine or with repeated "606," they conclude that the proportion of partial or complete failures is not greater than in a large series of cases, and that certain complete cures with "606" have been reported after extensive preliminary arsenic treatment. Further cases so treated and resistant to "606," have been cured by further exhibition of the very drug through which they have acquired tolerance. While many injections of "606" may result in a tolerance, such an issue is rare. In the discussion, it seemed to be the consensus of opinion that for obstinate cases 0.5 gr. followed after five days by 0.6, then by 0.7 for men, intravenously, then a rest for ten days, and further similar treatment of 0.5 and 0.6 gave the best results. This prevented rapid excretion and also tended against massive doses, so that the organism was continually saturated.

Importance of Testing for Isoagglutinins Before Transfusion.—OTTENBERG (*Jour. of Exper. Med.*, 1911, xiii, 425) relates experiments on isoagglutinins which are interesting in view of the increasing number of transfusions lately reported in addition to the number of treatments of severe anemias and hemorrhagic states with defibrinated blood. He records Schultz's recent observations on injections of defibrinated

blood in severe anemias where the first patient whose blood was hemolyzed and agglutinated by that of the donor suffered marked collapse, whereas those wherein there was not this reaction showed little or no effects in the majority of cases. He feels that intravascular agglutination may occur from the donor's blood, but that it may give rise to no symptoms. The process may be influenced by (1) concentration of the agglutinin; (2) absorption of the agglutinin by excess of the agglutinable cells; (3) interference with agglutination by excess of non-agglutinable cells whereby the clumps are made small. In case a non-agglutinative donor cannot be obtained, he feels it would be better to use a donor whose serum agglutinates the donee's cells rather than one whose cells are agglutinated by the patient's serum. He concludes that serum tests should be done when possible, but that as agglutinable cells are destroyed by phagocytosis, their use in transfusion is but slight.

Experimental Sarcoma of the Fowl.—PEYTON ROUS (*Jour. of Exper. Med.*, 1911, xiii, 397) reports progress with his transmissible sarcoma of the fowl. He has succeeded in producing the tumor in normal hosts by a cell-free filtrate passed through a Berkefeld filter. This growth from the cell-free filtrate has furnished tumors capable of producing new tumors after injection. The tumor is a spindle-celled sarcoma growing by amitosis. The transplantation from filtrate takes much longer to appear than that from grafts. It has now reached such a stage of malignancy that it can be transplanted to other varieties of chicken, but not in other species of animal. Metastases, too, are becoming much more frequent and larger.

Salvarsan in Syphilitic Meningitis.—DU CASTEL and PARAF (*Bull. et mém. Soc. méd. d. hôp. de Paris*, 1911, xxviii, 252) discuss acute secondary syphilitic meningitis arising in a patient who exhibited secondary genital lesions in September, 1909, and came in for mercurial treatment in February, 1910. After a clinical cure, in nine months she was readmitted with intense headache, vomiting, pain in the back, and constipation. She was rigid, with a slow pulse and a temperature of 103°. Kernig's sign was positive. The reflexes of the upper extremity were retained, whereas those of the lower were lost. There were secondary lesions in the mouth and hyperplasia of the cervical glands. Lumbar puncture showing a cell count of 53 per c.mm., and the Wassermann test being positive, she was given 0.4 gr. of "606," intravenously, and in thirty-six hours her temperature fell to normal, the headache disappeared, and one day later the cervical rigidity was gone. Three days later the return of headache and persistence of clinical signs caused the administration of 0.3 gr. intramuscularly. After two more days Kernig's sign was negative, but the reflexes were still abolished. While the Wassermann reaction was growing less marked daily, the cerebrospinal lymphocytosis persisted, and a threatened return of the Wassermann led to a further injection of 0.3 gr. of "606" intravenously, and benzoate of mercury treatment. Thus, three injections of "606" have led to a more rapid improvement of acute signs than would mercury, but have not been sufficient to reestablish reflexes, nor to suppress the cerebrospinal lymphocytosis, a more certain sign of meningitis than is the Wassermann.

Meningitis Following Lead Poisoning.—MOSNEY and SAINT GIRONS (*Bull. et mém. Soc. méd. d. hôp. de Paris*, 1911, xxviii, 252) report a case of left hemiparesis in an alcoholic, aged forty-eight years, a painter for thirty-five years. During the last thirteen years he had five attacks of colic, the last three in six months. In this last illness, they noted the hemiplegia associated with hyperesthesia to pain, but both were so transitory as to disappear in a week. The systolic pressure meanwhile fell from 200 to 150 mm. Hg, but there was a persistent increase in the cerebrospinal lymphocytes—68 per cm. The Wassermann reaction was negative in blood serum and cerebrospinal fluid. The lead intoxication thus led to paresis by meningitis. LOEPER and PINARD, in the same journal (1911, xxviii, 226), report a case of acute meningitis in an electrician, aged thirty-nine years, who had headache, vomiting, and constipation, with cervical rigidity, Kernig's sign, and exaggeration of reflexes. It is only in occupations allowing of massive head intoxications, *e. g.*, in electrical works or china factories, that these incidents are possible. The symptoms simulate those of tuberculous or syphilitic meningitis; but the absence in one of the bacilli (even on guinea-pig inoculation) and in the other of the Wassermann, together with history and the favorable outcome, renders diagnosis simpler.

SURGERY.

UNDER THE CHARGE OF

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A Plastic Method of Operation for the Closure of Fistulæ Coming from Internal Organs.—ABRASHANOFF (*Zentralbl. f. Chir.*, 1911, xxxvi, 186) says that the essentials for the closure of every fistula through which the contents or secretion of an organ escapes are the removal of the cause of the fistula and the closure of its edges by sutures, as in bladder and intestinal fistulæ. Unfortunately such a method is not always possible, as in those coming from the kidneys, liver, and lungs. Since 1900 Abrashanoff has been employing a method of his own. A sufficiently large flap is prepared from the neighboring tissues, but is best made of muscle. After freshening the surfaces of the fistula by a sharp curette, the point of the flap is introduced into the fistula to its bottom, so that the whole canal is filled by the flap. In order to prevent the displacement of the flap, it is sutured at different points to the margins of the fistula. Within a few days it adheres and gives

a foundation for connective-tissue formation, which fills up the remainder of the opening. The fear that the flap will cause a damming up of secretion was not justified by Abrashanoff's experience. In a man, aged twenty-seven years, after a stab wound of the chest, there developed an abscess of the lung, which was opened by incision. Ten months after the wound was received a fistula still persisted and communicated with the lung, as shown by bloody expectoration after probing it. The above operation was performed, and in three weeks it was completely cicatrized. It was still closed nine months after the operation. In a woman, aged twenty-three years, during a double salpingectomy for an adhesive pelvic peritonitis, the colon was wounded, and after one and one-half months there still persisted a fistula, 6 cm. deep. After two months it was closed by the same operation. The flap healed in and the escape of feces soon ceased. In an old empyema, operated on twice by Schede's method, there remained a cavity 6 cm. deep, which was filled by such a flap and thus healed.

Concerning the Question of Drainage of the Thorax.—TIEGEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 347) reports the case of a man, aged thirty-seven years, who was admitted to the hospital with a stab wound of the thorax, in an almost pulseless condition. The knife had penetrated the right intercostal space, had divided the second rib and the internal mammary artery, and had produced a deep wound in the upper lobe of the right lung. There was an extensive pneumothorax with a marked cyanosis. Under the administration of oxygen, which improved the dyspnea immediately, the wound was enlarged downward, the wounded vessels ligated, and the wound closed by exact suturing with silk. The skin and muscle wound was closed by sutures down to the lower angle, where an opening was left, three fingers' breadth below the original wound. Through this oblique canal a strip of iodoform gauze was introduced. On the third day there developed signs of a high grade of pneumothorax, when the tampon was removed and there immediately escaped a quantity of bloody exudate. The breathing, which had been troubled, superficial, and panting, immediately became quiet and deep. In the place of the gauze drain a rubber tube was inserted, which was provided with an improvised valve. Healing followed. As a result of this experience, Tiegel devised a more suitable apparatus for this kind of drainage, which is described in detail. He also provided that the inner end of the tube should lie in the lowest part of the cavity near the spinal column.

Clinical and Experimental Investigations Concerning the Function of the Stomach after Gastro-enterostomy and Resection of the Pylorus.—SCHÜLLER (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxii, 715) says that an anterior gastro-enterostomy at the fundus of the stomach with a wide anastomotic opening and an adjacent entero-anastomosis will not cause an alteration in the form, position, or outline on distention of the stomach. Since by the use of the *x*-ray it is seen that during the taking of food, the stomach contents do not pass into the intestine, it is concluded that the anastomotic opening does not interfere with the function of the stomach. The path taken by the

food after the gastro-enterostomy will depend chiefly upon the movements of the antrum and the permeability of the pylorus. Notwithstanding the gastro-enterostomy, a part of the food always goes through the pylorus, and the closure of the pylorus is the only guarantee of the continued patency of the anastomotic opening. In the normal stomach of a dog, a gastro-enterostomy made in the antral portion of the stomach will provide a more physiological evacuation of the stomach contents, and the opening tends less easily to become closed than when it is made in the fundus portion. It does not prevent, however, the partial passage of the food through the pylorus. For the exclusion of the duodenum, a gastro-enterostomy with closure of the pylorus is indicated. A simple retention from atony of the stomach and inflammatory tumors of the pyloric region, calls for a gastro-enterostomy in the fundus portion of the stomach without closure of the pylorus. In a gastropptosis without retention, a gastro-enterostomy is not to be recommended. When, during a gastro-enterostomy operation, an unhealed ulcer is found and is not excised, suitable diet and rest of the stomach must be provided. The evacuation of stomach contents through the anastomotic opening will be well toward the normal, but will not exceed the normal. This evacuation does not occur continually, but in jets, and goes mostly toward the efferent loop, rarely through the afferent. The cause of the interruption in the outflow of food is not to be sought in the stomach, but in the intestine. The removal or closure of the pylorus is not associated with as easy an evacuation of the stomach contents as is a simple gastro-enterostomy. The time for evacuation when the pylorus is closed varies. Retention in a resected stomach does not imply an insufficient anastomotic opening. This opening in such an operation should be placed at the deepest part of the stomach. A gastro-enterostomy almost always impairs stomach digestion. Without the evidence of lactic acid, a recurrent carcinoma in a resected stomach cannot be diagnosticated. There is no reason after a gastro-enterostomy to reduce the albuminous foods in favor of the fats. Digestive disturbances are to be treated as if no gastro-enterostomy had been done. The stagnation of the escaping stomach contents in the intestinal loop has only a subordinate influence on the development of a jejunal ulcer.

The Results and Prospects of Conservative Treatment of Hourglass Contracture of the Stomach, with a Contribution on the X-ray Diagnosis of the Same.—SCHLESINGER (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxii, 787) says that hourglass contracture of the stomach is generally considered a surgical disease and that it always calls for operation. According to his experience a certain diagnosis and the determination of the degree of the constriction is at times possible only by means of the Röntgen ray. For the differential diagnosis not only is the intermittently spastic contraction of the hourglass stomach observed, but what is more important the formation of folds within the stenosed area and continuously tetanic contraction are maintained by the presence of ulcers, erosions, and stagnation. Occasionally we are able to ameliorate these spasms by internal therapy and sometimes even to cause them to disappear. In this

way the gastric motility may be considerably improved. In cases of hourglass contraction in which such improvement is obtained in a few weeks operation is not necessarily indicated. In order that such patients while running a symptomless course may not get worse, regular examinations should be made at periods of from six to twelve months.

The Treatment of Fistulæ with Beck's Bismuth Paste.—BRANDES (*Deut. Zschr. f. Chir.*, 1911, cviii, 221) says that of 30 cases injected, in 29 it was with a therapeutic purpose, and in 6 of these without successful results. Of 4 thoracic fistulæ, in 3 the cure was surprisingly rapid. The fourth was a bronchial fistula; 7 other fistulæ of various kinds, excluding those arising from bone and joint disease, were healed. Of 18 fistulæ from bone and joint disease, with the exception of 3 cases of a tuberculous nature, 12 were successfully treated, 1 remained doubtful, and 5 were failures. Brandes regards these injections as an excellent improvement in the diagnosis of fistulæ by the x-rays. When the injections of bismuth are rationally carried out, they favor healing of the distended fistulæ and the time necessary to bring this about is remarkably short. Failures are to be expected by the method, the chief factors then being a markedly depressed general condition of the body, copious discharge from the fistula and a progressive primary disease process. Advanced bone and joint disease (Pott's disease and coxalgia) give the greatest number of failures. The method exposes the patient to the danger of bismuth and nitrite poisoning. This danger is much lessened by changes in the method, the substitution of bismuth carbonate for bismuth nitrite, and by diminishing the quantity of the bismuth paste employed. However, it has not been entirely eliminated. Non-poisonous substitute preparations must be found, which will have the same healing effect as the bismuth paste, so that we shall obtain not only a very rapid and successful method of treatment but at the same time one that is without danger.

An Experimental and Clinical Study of the Functional Activity of the Kidneys with the Aid of Phenolsulphonaphthalein.—ROWNTREE and GERAGHTY (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 284 and 414) say that the functional tests, together with a careful clinical study of the patient, furnish without doubt valuable information concerning the functional capacity of the kidney. The phenolsulphonaphthalein tests as they were carried out by the writers gave many advantages over all other functional tests proposed up to the present time. This preparation is much better adapted for a functional test than any other substance previously employed, because of its prompt appearance in the urine and its rapid and complete elimination by the kidneys. The quantitative estimation of the amount excreted is simple and exact. The permeability of the kidney for this substance is diminished in chronic parenchymatous nephritis as well as in chronic interstitial nephritis, the diminution being more marked in the interstitial variety. This test is shown to be of great value in revealing the real condition of the kidneys of patients presenting a urinary obstruction of prostatic origin. It has in these cases greater value than the study of the total quantity of the urine and the total quantity of solid matter or urica,

and it permits the surgeon to choose for operation a time when the kidneys are in a satisfactory functional condition. The amelioration observed in these cases of prostatic obstruction from the institution of preliminary treatment is demonstrated in a remarkable manner by the phenolsulphonaphthalein test, which indicates also the favorable time for operation. In renal lesions, unilateral or bilateral, the absolute amount of work done by each kidney and the relative proportion of work of both kidneys, can be determined when the urines are taken separately.

Operative Treatment of Wounds of the Heart.—BREWSTER and ROBINSON (*Annals of Surgery*, 1911, liii, 324) report a case of gunshot wound of the heart with autopsy following operation performed when the patient was almost moribund, and have made a study of the subject. The reported cases of wounds of the heart show that 71 cases have been successfully sutured, while 106 have been operated on with fatal result; 11 of the recoveries and 13 of the failures were cases of bullet wound. As the operation is still in a comparatively new field of surgery, and is looked upon as a considerable achievement, it is probable that a large proportion of the successful results have been reported. If, however, some of the failures have not been reported, the mortality of 60 per cent., which the above cases show may be an unduly low one. The writers regard the diagnosis of heart wounds as usually difficult, and that they rarely exist without pleural or lung involvement. Operative rather than expectant treatment is indicated in a large proportion of the cases. Osteoplastic flaps should not be employed. Intercostal incision, with or without subsequent division of ribs, is the preferable method of approach. In certain cases the heart wound may be of sufficient size to permit violent hemorrhage at the time of suture. In such cases interrupted manual compression of the superior and inferior cavæ may be a possible safe procedure; the profuse hemorrhage without this compression is of greater danger. Differential pressure with apparatus is by no means a *sine qua non* in all operations for wounds of the heart and lungs. It is, however, a valuable agent to control the respiratory function, to regulate the heart beat, and to reinflate the lung at the end of operation. Air tight closure of the pleural cavity with reinflation of the lung should be employed when possible; the intercostal incision followed by a pericostal stitch is a successful method of securing tight closure. Drainage of the pericardium is unnecessary.

Clinical and Pathological Significance of Obliteration, Carcinoma, and Diverticulum of the Appendix.—McCARTY AND McGRATH (*Surgery, Gynecology, and Obstetrics*, 1911, xii, 211) say that the character and significance of obliteration of the lumen of the appendix have been very much disputed since it was first described. The condition was considered a normal physiological involution, by which the organ itself was disappearing. The majority if not all pathologists now consider the process the result of infection. The writers studied microscopically 5000 specimens in relation to obliteration, carcinoma, diverticulum, inflammation, and foreign bodies, the material being furnished by the clinics of Drs. W. J. and C. H. Mayo, and E. S.

Judd, St. Mary's Hospital, Rochester, Minnesota. This series confirms the percentage of obliteration found in the appendix by other observers. Obliteration seems to occur as the result of an inflammatory process as shown by the histology, the time of occurrence, the duration of the process, and the higher frequency in appendicitis than at autopsy in general. Many appendices become acutely inflamed during the process of obliteration and, therefore, an obliterated appendix should be removed if possible. Carcinoma may occur at practically any age. It was impossible to make the diagnosis of carcinoma from the external appearance in 77 per cent. of the cases of carcinoma. The high frequency of carcinoma in obliterated or partially obliterated appendices may demand removal of all partially or completely obliterated appendices. Carcinoma of the appendix occurs in association with changes in the appendix which are related to the process of obliteration. Carcinoma of the cecum probably arises from the appendix only in a very small percentage of the cases.

THERAPEUTICS.

UNDER THE CHARGE OF

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Salvarsan Therapy: An Answer to Ehrlich.—FINGER (*Wien. klin. Woch.*, 1911, xxiv, 65) says that a satisfactory explanation for the untoward results after the use of salvarsan has not yet been offered. They may not be due to the remedy, but this should be definitely proved before salvarsan is used in general practice. Besides this, the technique of administration, dosage, and indications must first be more definitely determined. He believes that Igersheimer's conclusions that salvarsan cannot harm a healthy eye because it seems to cure syphilitic eye lesions is too broad, because the action of salvarsan on a healthy optic nerve may be quite different from its action on the diseased nerve. Finger also makes use of Martins' findings of extensive necrosis at the point of intramuscular or subcutaneous injection. Martins found this necrosis present in every one of 12 patients examined within two or three weeks after the injection of salvarsan. Finger apparently does not take into consideration that these findings may well indicate that injections should be intravenous as Ehrlich recommends. In general, it may fairly be said that Finger's objections in this article are not real and do not differ really very much from the view often expressed by Ehrlich himself.

By-effects of Salvarsan.—FINGER (*Wien. klin. Woch.*, 1910, xxiii, 1667) writes concerning four serious eye effects that he attributes to salvarsan. In one patient the salvarsan had been injected two months

after the primary infection. She returned to the clinic two months after the injection complaining of headache, vertigo, and impaired vision in the right eye. She was found to have paralysis of some of the ocular muscles of the right eye and early optic neuritis on the left side. She was given another injection of salvarsan, followed by mercury and iodide, but there has been no improvement, and the right optic nerve finally showed signs of neuritis. Another of his patients, three months after the injection, showed evidences of right peripheral choroiditis with central turbidity of the vitreous. A third patient, also three months after the injection, and five and one-half months after the initial infection, returned to the clinic with abducent paralysis that Finger denotes as an extremely rare occurrence so early in the disease. The last case of this series was one of malignant syphilis, who showed great improvement after the injection of salvarsan, although actively treated previously by the usual methods, including arsacetin and enesol. She returned to the clinic with eye symptoms three months after the injection, and the examination of the eyes showed beginning optic neuritis. Finger implies that cases of choroiditis, paresis of the ocular muscles, and iritis reported by Wechselsmann as unusual forms of syphilitic recurrence are really of toxic origin. He also mentions Fischer's cases of iritis and neurochoroid retinitis. Finger also reports three cases in which the auditory nerve seemed to be affected. One patient had nystagmus, vertigo, and a typical tendency to fall, with intact hearing. These symptoms, however, were transient, but in two other cases deafness and vertigo have persisted. He notes that in these 3 cases the Wassermann reaction has been repeatedly negative. It is rather interesting that, in the patient with transient symptoms the symptoms came on the day after the injection, although in the other two cases the symptoms developed nine weeks and four months after the injection.

Antihemolytic Action of Arsenic.—GUNN and FEETHAM (*British Med. Jour.*, 1911, 2612, 137) relate rather interesting experiments, from which they draw the following conclusions: Arsenic, whether in the form of sodium arsenite or sodium arsenate, exerts on the red blood cells an action antagonistic to that of certain hemolytic agents. The experiments, therefore, afford additional proof that a protective action on the formed red blood cells against normal or abnormal hemolytic processes may, in part at least, account for the as yet imperfectly explained benefit which results from the medicinal administration of arsenic in blood diseases.

Technique for and Action of Salvarsan.—EHRLICH (*Deutsch. med. Woch.*, 1910, xxxvi, 2437), in a communication reported by Daschinsky, says that subcutaneous injections have the disadvantage of causing pain and infiltrations. A more marked objection to their use is the uncertain absorption of a given dose. He also believes that an emulsion is the most unsatisfactory preparation of all, chiefly because of slow absorption, possibility of abscess formation, and late untoward results. An important reason for proving the intravenous method is that the dose may be repeated if necessary. This is often unwise if the first injection has been made subcutaneously or intramuscularly and

left a large depot of arsenic in the tissues. Careful attention should be given to syphilis not older than from two to eight months. Salvarsan should be given systematically and the patient kept under careful supervision, especially after the tertiary stage, in order to combat the army of spirochetæ with success. Ehrlich says that if salvarsan be not given in this careful method it is better not to give it at all. He adds that the curative action of salvarsan has been established not only in syphilis, but in tertian malaria, sleeping sickness, smallpox, spirillosis in animals, kala-azar, etc.

Salvarsan in Malaria.—IVERSON and TUSCHINSKI (*Deutsch. med. Woch.*, 1911, xxxvii, 107) draw the following conclusions from their observations as to the effect of salvarsan in malaria: (1) Salvarsan administered intravenously in a dose of 0.5 gram exerts a specific action on all varieties of malarial parasites. (2) In the tertian form the parasites leave the blood in from twelve to forty-eight hours. It has not been determined that this effect is permanent, however. It may be advisable to combine the intravenous method with the intramuscular. (3) In the quartan form, the effect obtained is not permanent even with injections as high as 0.8 gram. (4) In the tropical form, doses of from 0.5 gram to 0.8 gram free the peripheral blood of the ring forms only transiently. (5) Crescents do not disappear, although somewhat altered in their shape and staining properties. (6) A few cases of tropical malaria, show after a short period of improvement, a considerable aggravation of all the symptoms.

Experiences with Salvarsan in the Treatment of Syphilis.—PORT (*Med. Klin.*, 1911, vii, 452) says that the subcutaneous injection is objectionable for many reasons. He has seen numerous instances in which a deep necrotic process developed at the site of the injection. The technique of the intravenous injection is complicated and is not fitted for general practice. The injection itself must be carried out absolutely correctly because of the danger of thrombosis and embolism that exists even with the best of technique. On account of the danger of such disturbances the injection is made in the left arm. Port believes that salvarsan is an advance in the chemical treatment of syphilis. It is of especial value in the treatment of so-called malignant syphilis and those cases that are refractory to mercury and the iodides. A single intravenous injection seems to be usually insufficient to completely subdue syphilis. The final effect of repeated intravenous injections is not fully determined. Since the introduction of salvarsan many symptoms referable to the cranial nerves have been observed. Port believes that these are to be considered as toxic manifestations, produced not only by the endotoxin, but also by salvarsan. He thinks that the most suitable treatment of syphilis at the present time is a combination of salvarsan with mercury.

Treatment of Hookworm Disease.—STROSNIDER (*Jour. Amer. Med. Assoc.*, 1911, lvi, 1027) discusses the symptomatology and the effects of hookworm disease and advocates the following plan of treatment. Ground itch in the papular or vesicular stage may be treated with a 5 per cent. salicylic acid suspended in collodion. During the pustular

stage the wounds should be cleansed and cauterized with silver nitrate and then a dry dressing of 5 per cent. boric acid and zinc oxide ointment applied twice daily. When great swellings occur, hot applications should be used. To allay itching and prevent secondary infection, a combination of 5 per cent. zinc oxide and salicylic acid ointment, applied locally and twice daily, is recommended. It is important to keep the foot bandaged or covered to prevent scratching or rubbing. The internal treatment should be begun on the fifteenth day from the date of the ground itch and repeated once. The same treatment should be instituted after an attack of ground itch as if eggs of the hookworm were present in the stools, thus getting rid of the worms before they reach maturity and have done much harm. The stools should be examined at the end of six and twelve weeks from the attack of ground itch for eggs of any worm that may have escaped previous treatment. The first step is to remove the protecting chyme and mucus by a large dose of salts—Rochelle, Epsom, or Glauber's—four hours after the last meal. Sodium sulphate dissolves and removes the intestinal mucus best. The drugs employed to kill or expel the worms are thymol, betanaphthol, and male fern. The dose of thymol for children should be in proportion to the size, apparent age, and physical condition. Strosnider has been giving about 2 grains per year up to the age of thirty, the same to be administered in two equal doses two hours apart. Unfavorable conditions, such as great weakness, extreme anemia, diarrhea, cardiac depression, pregnancy, and dropsy, require a smaller dose. Thymol should be given in two or three broken doses to prolong its presence in the upper bowel. Because of its tendency to pack together under pressure or in the mucus of the intestine, equal parts of sugar of milk or some other soluble substance should be mixed with it. To prevent burning of the mouth and throat, it should be given in cachets, wafers, or capsules; it may also be given suspended in either mucilage or syrup of acacia, or some simple syrup. The patient should lie on the right side and refrain from drinking much water, to prevent vomiting. After two or three hours another brisk purgative of salts (never castor oil) should be given to prevent its absorption. The patient should remain in bed during the treatment. No food or drink, except water, should be allowed from the time the preparatory purgative is given until the purgative following the thymol has acted well. If the patient is weak or faint, or if the burning in the stomach is excessive, a little warm coffee may be allowed. The diet need not be restricted after several free movements have occurred following the post-thymol purgative, unless there is some special indication. The treatment should be repeated once a week until examination of the stool is negative. Oils, fats (milk or butter), patent medicines, or beverages containing alcohol should not be allowed during thymol treatment. Thymol may affect the patient in one of three different ways—by intoxication, by irritation of the kidney, and by irritation of the stomach and intestine. The symptoms of thymol absorption are depression, headache, weakness, dizziness, tinnitus, nausea, unconsciousness, rapid, weak pulse, and sometimes profuse sweating and subnormal temperature. Thymol occasionally causes epigastric pain, nausea, and vomiting, and more or less diarrhea. Therefore, gastritis and diarrhea or dysentery are

contraindications to its use. Half the usual dose should be given to feeble patients.

The Effects of Digitalis upon Irregular Heart Action.—EDENS (*Therap. Monatshefte*, 1911, xxv, 1) says that the best results of digitalis are obtained in cases of mitral disease associated with a deficient heart muscle. These results are probably due to an improved coronary circulation resulting in better nutrition to the heart muscle. Digitalis, on the other hand, fails in those cases in which the irregular and rapid heart action is due to nervous influences. Notable examples of this are paroxysmal tachycardia, and the rapid pulse of Graves' disease. There are certain cases of extrasystole dependent upon organic changes that react very favorably to digitalis. However, when extrasystoles are the result of disturbances in conductivity, digitalis will usually fail. He therefore suggests that perhaps digitalis may be of value in differentiating the varieties of extrasystole. Edens thinks that the newer methods of diagnosing the elements at fault in the maintenance of normal cardiac action have proved the beneficial action of digitalis in suitable cases of cardiac disease. He includes in his article interesting cardiograms, showing the effect of digitalis upon a number of cases of various types of heart irregularities. In one case of atrioventricular extrasystole, Edens administered the drug intravenously, and instead of producing an improvement in the condition, an increase of extrasystoles occurred with collapse, but this was not the case when the drug was given by the mouth. Edens also refers to the occurrence of pulsus bigeminus during the use of digitalis, and to what has been called pseudoalternans.

Hypodermic Injections of the Salicylates in Rheumatism.—SEIFERT (*Med. Record*, 1911, lxxix, 432) advocates for the treatment of acute rheumatic infections of joints, heart, pericardium, pleura, and central nervous system (chorea) injections of 10 c.c. of a 20 per cent. sterilized solution of sodium salicylate to 100 pounds of body weight. This is injected fifteen minutes after the injection of an appropriate cocaine solution. If the injections are made earlier than this they cause considerable pain. This dose should be repeated every twelve hours. In severe cases with multiple lesions he advises an increase of the dose to 15 c.c. of the solution to 100 pounds body weight. Smaller doses than these will be without effect. Joint stiffness, pain, fever, and pulse rate diminish and the general condition of the patient improves, he says, within three hours after the first injection. If the injections are continued regularly every twelve hours, the improvement also continues; but if they are omitted for twenty-four hours in severe cases, the symptoms will grow worse. In the milder cases the improvement may continue even without a repetition of the dose. In chronic cases 10 c.c. to 100 pounds of body weight of the following oily solution are injected every twenty-four hours. This mixture contains salicylic acid, 10 grams; sesame oil, 80 grams; pure alcohol, 5 grams; and gum camphor, 5 grams. This oily solution is sterilized before the alcohol is added, but must not be exposed to the air, as the alcohol will evaporate and the salicylic acid crystals will precipitate. The effect of the injection in chronic cases is obtained more rapidly

when multiple localizations of the rheumatic process are present than when one joint is affected. In the former, pain and stiffness usually improve after the first injection; in the latter, after the third. The addition of camphor (from 5 to 20 per cent.) has been found beneficial in stimulating the heart when the pericardium or the endocardium is involved. One of the chief advantages of this method is the entire absence of all the toxic symptoms that are sometimes seen when salicylates are given by the mouth. Leibert gives the details of the technique of this procedure in his article, and states that he has seen no local or general untoward effects resulting from the injections.

The Treatment of Gout and Rheumatism with Radium.—His (Berl. klin. Woch., 1911, xlviii, 197) gives his results with the radium treatment of 100 cases of chronic rheumatism and 28 cases of gout. Forty-seven were improved, 29 considerably improved, 5 cured, 13 were uninfluenced by the treatment, and in 6 no result was apparent. He adds that the majority were severe cases that did not respond to other methods of treatment. He gives the details of some of these cases. The best results occurred in the early stages of the disease. Of the 28 cases of gout only 4 were unimproved, while 24 were markedly improved, some completely cured. The differential diagnosis between chronic rheumatism and gout was made by the determination of the uric acid content of the blood. His says that the action of radium was very striking upon the amount of uric acid in the blood. Usually within a few weeks the uric acid in the blood diminished remarkably. In a few cases this same result occurred within a few days. In general this diminution of the uric acid in the blood was associated with the clinical improvement. His observed that tophi in the ear disappeared on two occasions during the treatment. A marked clinical improvement was noted in a patient with no change in the amount of uric acid in the blood. On the other hand, in another patient who had gouty nodules all over his body, no uric acid was present in the blood either at the beginning or toward the end of the treatment, and yet the patient had repeated attacks during the whole time. His recommends the inhalation of radium emanations for two hours daily as the most satisfactory method of treatment. Others have also advised the injection of solutions of radium in the neighborhood of the affected joints. His does not believe that radium is specific in gout, but that it is most useful in certain cases. No result is to be expected in patients with bony ankylosis. His says that a more accurate standard of dosage that can be used to compare the results of different observers would be of great value in this method of treatment.

The Treatment of Tuberculosis by Deep Muscular Injections of Mercury.—WRIGHT (*New York Med. Jour.*, 1911, xciii, 513) says that during the past three years he has reported several hundred cases of chronic tuberculosis successfully treated by injections of mercury. He believes that his reported cases sustain his view that mercury has a direct destructive action upon tubercle bacilli, and that it is profoundly antitoxic in this disease. He says that the cases reported by himself and others demonstrate the fact that tubercle bacilli have a strong affinity for the succinimide and bichloride of mercury.

He has seen a number of cases in which three or four injections of one or the other of these salts caused the tubercle bacilli to disappear from the sputum and the feces, and the cessation of the most profound toxemia. He reports in detail a case diagnosticated as acute miliary tuberculosis that terminated in an apparent cure. In less than eight weeks after the onset of the disease, at a time when 95 per cent. of these patients are either dead or dying, and six weeks after the administration of the first injection, the patient was apparently cured. Wright thinks that this case warrants the belief that in mercury we have the chemical affinity of the tubercle bacillus, and the hope that experimentation will sooner or later develop a compound of mercury for which these organisms will have even a stronger affinity than they display for the succinimide.

PEDIATRICS.

UNDER THE CHARGE OF

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Purpura in Childhood with Fatal Cerebral Hemorrhage.—FEDOR SCHMEY (*Deutsch. med. Woch.*, 1911, xxxvii, 307) reports a case of purpura in a child, aged eight years, with fatal termination from cerebral hemorrhage. Cerebral hemorrhage in purpura is very rare, such an authority as Hensch having reported but one case, which developed convulsions, stupor, and hemiplegia. Schmey's case occurred in a well-developed and apparently healthy boy. When seen on October 10, the boy had been spitting up blood for several preceding mornings, and the cervical glands on both sides were swollen, but not tender. There was harsh breathing over the apex of the right lung. Physical signs were wanting to show that the blood came from the lung. There had been recent bleeding from the gums. There was prostration, but no pain. The temperature remained normal, and there was no swelling or tenderness of the joints. On October 12 there was vomiting of dark blood mixed with stomach contents. On October 15 there appeared on both legs and on the right arm about twelve dark patches the size of a penny. These patches were clear, black, round, did not disappear on pressure, and had a central elevation. On October 18 a sudden coma developed. The pupils were dilated and did not react, and the reflexes of the conjunctiva and skin were absent. The liver was enlarged to the level of the umbilicus; the pulse was slowed, but regular; and the gums were covered with small hemorrhagic areas. The temperature was 39.5° C. The coma continued until death occurred, four hours later. Convulsions did not appear, either preceding or during the coma. Shortly before death there occurred a severe hemorrhage from the mouth. These symptoms indicate a fatal cerebral hemorrhage and an extravasation into the brain substance. This case

seems to stand between a purpura abdominalis and a purpura hemorrhagica, and does not conform entirely with any of the four forms as laid down by Henoch. It also shows that purpura is not a disease sui generis, but a number of processes combined in an uncertain manner, all having the tendency to produce bleeding from the skin, mucous membrane, or the parenchyma of organs. Infectious diseases seem to have a bearing on the development of purpura. The case just described had had scarlet fever two years before. Henoch's case had scarlet fever four years before the purpura. Schmey places more weight upon the fact that the child suffered from a scrofulosis, probably tuberculous. Wolf lays stress on an inherited tuberculous taint in the etiology of his cases. He also observed that bleeding began in the erect position, but disappeared in the recumbent. In Schmey's case the bleeding developed seriously after the child had been in bed for several days.

The Recognition of Eosinophilic, Intestinal Crises in Infants.—LEO LANGSTEIN (*Munch. med. Woch.*, 1911, lviii, 623) some years ago reported a condition in infants in which there occurred sudden discharges from the bowel of mucus and pus in which were found large numbers of eosinophile cells. In the absence of an alimentary or infectious bowel disturbance this condition was thought to be a partial manifestation of that symptom complex which Czerny has named an "exudative diathesis." In both of Langstein's cases symptoms of this condition were present. Czerny and Goeppert have expressed their belief that the mucous membrane of the intestine frequently shares in the manifestation of the exudative diathesis. Since then, Langstein had made a study of mucopurulent stools in infants to determine the frequency of eosinophile cells, and found the condition much more frequent than was supposed. He believes this is one of the early symptoms of the exudative diathesis. He describes a typical case in a baby aged five weeks, which developed facial eczema, and a few days later sudden copious, mucopurulent stools containing eosinophile cells in great numbers. These stools continued for two more days and ceased as suddenly as they began. The eczema became worse during this time, and the body weight diminished only slightly. There was no rise in temperature, and the blood showed an eosinophilia of 8 per cent. In this case, alimentary and infectious disturbance of the bowels being ruled out, and the view taken that the condition was a manifestation of an exudative diathesis, as shown by the eosinophile cells and the stools, no change was made in the infant's nourishment except a slight reduction in quantity. The presence of the eosinophile cells, therefore, is not only of diagnostic value, but is a guide to our regulation of the nourishment. In these cases it is unnecessary to employ a starvation diet, as in infectious and alimentary bowel disorders; and fever and loss of weight are not found as in the last two conditions.

Neurasthenia in Older Children.—CLIVE RIVIERE (*The Practitioner*, 1911, lxxxvi, 46) accepts Savill's division of neurasthenia in older children into the etiological factors of toxic malnutrition and fatigue neurasthenia, and that due to shock and traumatism. As a rule, the causation is mixed. Neurasthenia in older children is usually

a fatigue, or exhaustion, neurasthenia due to overpressure in a nervous subject. Malnutrition and dyspepsia may be combined, but are generally subsidiary. Overpressure combined often with deficient sleep is the largest factor. The symptoms are a mixture of cerebral, spinal, cardiac, vasomotor, and gastro-intestinal conditions. These are characterized by poor concentration, headache, insomnia, and fatigue. Obsessions and "phobias" may appear, and irritability and emotional attacks. Physically there appear loss of appetite and of muscular energy, wasting, and cardiac palpitation. At times there occur incoördination of muscular movement, such as habit spasm, stammering, finger twitching, etc. The backward children suffer from overpressure in the elementary schools, but the bright, precocious children in upper class schools. This pressure to win distinction in school can only be harmful, and leads to neurasthenia. The causes of overpressure are numerous. Within the school overlength of individual tasks and overlength of time in school are the important factors. Dr. Clement Dukes allows six hours per week at the ages of five to six years, nine hours at six to seven years, and twelve hours at seven to eight years, but such moderation is rarely practised. Other factors are deficient ventilation and lighting, bad arrangement of tasks, and defects in vision and hearing. Outside the school excess of home work, often amid noise and distraction, holds first place, especially when increased by private lessons in music or foreign languages. These causes are more potent when there exist predisposing causes, such as malnutrition, postfebrile debility, puberty and rapid growth, and insufficient air, exercise, and sleep. Insufficient sleep itself is a potent cause, and in addition to the difficulty in sleeping found in neurotic children the excitement from entertainments and home work at night is conducive to insomnia. The treatment of the neurasthenic boy or girl is the removal of the cause, whether overpressure, want of sleep, or both. Change to country air and pursuits, a quiet life, long hours out of doors, long hours in bed, cold bathing, and supervision of the digestive organs will usually result in a cure. Sufficient time must be given for complete recovery. A tendency to relapse may remain, and a return to former occupations must then be gradual. Some cases will not return to that condition which admits of a strenuous life, and these must have a carefully planned-out life, with work of a different kind, preferably physical. However, physical exertion carried to excess will induce disastrous results as surely as will brainwork.

A Record of 90 Diphtheria Carriers.—ANGUS G. MACDONALD (*Lancet*, 1911, clxxx, 795) reports the result of a bacteriological investigation of diphtheria in the borough of Crewe during a period of six months. Examination was undertaken on account of contact with a notified case of diphtheria, the "contacts" being roughly divided into "home contacts" and "school contacts." The matter presented is limited to the carrier problem, which must be regarded as an important factor in the spread of the disease. The situations examined for the presence of bacilli were the nose and throat, and occasionally the ear. During the period of six months there were 157 notified cases of diphtheria on the borough. There were 534 "home contacts" examined, of which,

62 were positive. There were 644 "school contacts" examined, of which, 28 were positive. Therefore, a total of 1178 contacts were examined, with 90 of them positive. The chief point here is the proportion of contacts found positive to contacts examined, and the relative proportion of positive home contacts to school contacts. All school carriers were found intimately associated at play with other cases and carriers. Classroom proximity was found of little importance in spreading the disease. In the home the positive cases were found in greatest number among those in closest communication, the same holding for playmates in the street and at school. This evidence shows the very intimate means necessary for the transmission of diphtheria, and indicates how readily this progress may be prevented by bacteriological examination and detection of positive cases. This series of 90 carriers exhibits four definite groups: (1) Those showing no clinical evidence of diphtheria and in whom the bacillus is found for a short time; (2) those giving a history of "cold," "sore throat," "mumps," etc., some time previously. They may exhibit paralysis and are neglected cases of diphtheria; (3) cases without a clinical history but with some local lesion of the throat, nose, ear, etc., where the bacillus lodges; (4) those who have had a definite attack of diphtheria and in whom the bacillus remains for long periods after convalescence. The fate of the bacillus when it disappears is not obvious. It probably disappears before the growth of some other organisms developing in that environment. However, experiments in implanting organisms inimical to the bacillus have so far been unsuccessful. Antitoxin has no apparent effect on the persistence of the bacillus in carriers any more than in cases. The length of carrier life seems to have no effect on virulence, bacilli being virulent after four and eight months in the nose and ear. Carriers occur most among intimate associates, mother or nurse and child, child and child at play. At school the carriers found are few and always closely associated with some other carrier or case, usually at play. The control of diphtheria depends on controlling the carrier. All carriers should be notified as diphtheria, quarantined, and observed until the disappearance of the bacillus. There is a slow, inevitable distribution of the disease persisting endemically in the carriers.

Etiology of Poliomyelitis.—A. E. VIPOND (*British Med. Jour.*, 1911, No. 2620, p. 612) draws a new conclusion as to the etiology of poliomyelitis from observations made on 16 cases of the disease. He remarks that Flexner established the infectious nature of the disease, and from his experiments it is shown that the inoculation time is practically the same as in typhoid fever. The virus passes through the finest filters, but sections and film preparations have failed to show bacterial or protozoal parasites as causing the infection. He quotes Holt as to the frequency of finding two or more cases in the same family. In 37 of the cases the interval between the first and second cases was ten days or less. This points to the contagious nature of the disease. The above conditions appearing in his own cases led to the thought of similarity between typhoid fever and poliomyelitis. Both diseases occur in the late summer and fall months, becoming almost extinct during cold weather. Diarrhea is just as

common a symptom in poliomyelitis as in typhoid fever. The incubation period is practically the same in both diseases. Flexner found it thirteen days experimentally, and Holt ten days clinically, in poliomyelitis. Both diseases are prevalent in cities where and when the cause of typhoid fever is traceable to the water and milk supply. They are both less frequent where the water and milk are pure. It is practically the same degree of contagion. These observations suggested the same character of organism as in typhoid fever. In blood examinations in cases of poliomyelitis he found the Widal reaction present as in typhoid fever, proving to him conclusively that the disease is from the same source and that the germs of the two diseases are allied. He asserts that the precautions used to prevent typhoid fever will have the same effect on the spread of poliomyelitis. He examined for the Widal reaction the blood of 13 cases of poliomyelitis, and 3 normal cases of members of infected families to prove the Widal reaction was not a family peculiarity. The Widal reaction was positive in 6 cases, highly suggestive in 4 cases, and negative in 6 cases, among which were the 3 from the healthy individuals. Out of the 3 negative results in the affected cases, 2 were obtained from cases of poliomyelitis from two and one-half to three months after the onset of the disease, and both were mild cases. This compares fairly well with the results found in an equal number of typhoid fever cases. Typhoid fever attacks the adult's weakest part, the intestine. Poliomyelitis attacks the most vulnerable part of the child and infant, the nervous system. The blood specimens in this series were examined by physicians making a specialty of that work. When a specific serum shall have been perfected, Vipond would make, as indications for its employment, a suspicious case with a positive Widal reaction. This should have the effect of modifying or preventing the disease.

Slight General Enlargement of the Thyroid Gland in School Children.
—C. W. HUTT (*Lancet*, 1911, clxxx, 875) calls attention to the number of cases of slight enlargement of the thyroid gland found in the examination of school children. The enlargement was not connected with anemia, mental hebetude, increased pulse rate, fine tremor of the hands, or exophthalmos. There was no pain or tenderness. In the district of Warrington, out of 3982 males examined, 37 showed enlargement of the thyroid. Out of 3787 females, 62 showed enlargement. According to the tables on the age in these cases the condition is not most frequent at the age of puberty, as 72 cases of the 99 occur below the age of thirteen. The above figures seem to show that the cause of enlargement in a large proportion of cases lies elsewhere than in the incidence of puberty. The water supplying the above district is a hard water, carrying, per gallon, calcium carbonate, 8.14 grains; magnesium carbonate, 2.63 grains; sodium chloride, 2.64 grains; and the total mineral salts running 15.06 grains per gallon. It is not known whether this quality of water has any effect on this condition, as it is supposed to have in the Alps. Out of 6 families of affected children examined, 3 showed a similar enlargement of the thyroid in several other members of the family. In one family of 9 people, 8 were affected. Hutt suggests that observation of this condition in the course of routine medical inspection of school children might throw light on the etiology.

OBSTETRICS.

UNDER THE CHARGE OF

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Cesarean Section or Pelvic Section.—PANKOW (*Ztschr. f. Geburt. und Gynäk.*, 1910, lxxvii, Heft 1) reports from the Freiburg clinic 7 cases of hebostiotomy in primiparæ, 2 cases of symphysiotomy; 11 cases of hebostiotomy in multiparæ, and 1 case of symphysiotomy. While the results with the mothers could be considered good, in the 21 children, 5 were lost—a result which can scarcely be considered satisfactory in comparison with other operations. When the life of the child is in danger, pelvic section in both primiparæ and multiparæ is not to be chosen. With primiparæ, operative delivery some hours after pelvic section, when the head has descended, is always a dangerous operation accompanied by severe lacerations of the soft parts. The writer would not perform pelvic section in the case of primiparæ because of the danger of lacerations in the subsequent delivery. In the case of multiparæ the situation is different, but even then the operation should not be undertaken when the child is evidently in danger. It is Pankow's belief that injuries to the bladder followed by incontinence, are a common result in this operation. It is his conclusion that pelvic section should be undertaken in multiparæ only when the head of the child, with its greater segment has entered the pelvis, so that the greatest circumference of the foetal head has descended well below the superior strait and the head can evidently pass through the pelvis readily, with a separation of the pelvic halves of not more than two fingers' width. Especial care must be taken to avoid instrumental delivery after pelvic section when the head of the child has not descended deeply into the pelvic cavity. In view of these complications, the old open method of symphysiotomy, devised by Zweifel, is superior to hebostiotomy because the formation of hematmata and thrombi is less frequent, while the results from the scar are better and give a better union for the patient than after hebostiotomy.

In choosing between suprasymphyseal and classic Cesarean section, the decision must be made as to whether the danger of opening the tissues about the symphysis, or the danger following opening the abdomen, is greater. Pankow's experience embraces 44 classic Cesarean sections, 3 by Frank's method, 36 cervical sections, and 5 extraperitoneal. Among these there were 5 maternal and 6 foetal deaths. One mother died from lumbar anesthesia with stovain; while in the classic section, 1 clean case, and 1 infected case, perished; in the cervical section, in addition to the death from necrosis there was one death from infection; while in the operation by Frank's method, there was one death in an infected patient. His conclusions concerning Cesarean section are that the classic Cesarean section should be reserved for cases of placenta prævia, as this operation gives the best access to the placenta with the least danger of thrombosis. In contracted pelvis the intraperitoneal cervical

section should receive preference. As regards the choice of operation for clean and infected cases—in clean cases the classic intraperitoneal and extraperitoneal cervical section can each be chosen, although the intraperitoneal operation is best. In multiparæ, with the child in good condition and presenting favorably, open symphysiotomy may be performed where the head is low down and can readily be delivered. In unclean cases, where labor has persisted long after rupture of the membranes, and the patient has been examined with unclean hands, the wish of the parents must be considered as far as possible. If they greatly desire a living child, intraperitoneal cervical section should be performed. In multiparæ with favorable presentation, pelvic section may be chosen. In infected cases when there is fever or foul amniotic liquid, a classic conservative Cesarean section has no place. Pelvic section should also be declined. If the child is dead or dying, cranioclasia should be chosen; and if the child is living, a Porro operation should be performed. Cranioclasia is indicated because with infected amniotic liquid and prolonged labor, the child almost invariably inspires so much infected material that septic pneumonia speedily develops. The wish of the parents for a living child may be consulted if they will permit the Porro operation. Where the indication for Cesarean section is absolute in infected cases, the Porro operation is to be selected.

Death after Early Rising in the Puerperal Period.—SCHERER (*Zentrbl. f. Gyn.*, No. 44, 1910) reports from Barsony's clinic, in Budapest, the results observed in allowing patients to get up early in the puerperal period. The method was not employed in those who had an especially severe labor, with fever before or after labor, and a severe delivery after some operation. He reports the case of a patient who had an incomplete abortion between the second and third months, and who reported that she had severe bleeding two days before admission. As there was foul discharge, she was given an intravenous injection of a 3 mg. sublimate solution. The uterus was emptied of its débris and irrigated, and the intravenous injection repeated. The first three days of the puerperal period were normal, with normal pulse and temperature. On the fourth day the patient was allowed to sit up beside her bed for half an hour. This was followed by some abdominal distention without tenderness, for which castor oil was given. She also received another intravenous injection of sublimate. In the evening she had fever, with rapid pulse and foul discharge, and had vaginal douches of potassium permanganate three times daily, with the use of an ice-bag. The patient developed streptococcus infection and hemolytic streptococci were found in the blood. She had frequent chills and high fever and was treated by various methods, including the irrigation of the vagina with 50 per cent. alcohol. Swelling of the left lower extremity developed, with tenderness over the femoral vein. The patient also developed pneumonia, and died on the sixtieth day. Autopsy showed a widespread streptococcus infection with thrombosis and metastases in the lungs. In 9257 cases of labor in the Budapest clinic there had been 34 cases of thrombosis, or 0.36 of 1 per cent. In two of these patients pulmonary embolism was a complication; one of these, a septic case, died. In 200 patients in whom the early getting-up was tried there

was one death from thrombosis—an occurrence which does not speak favorably for the early getting-up of the patient.

Air Embolism During Labor.—CAMPBELL (*Brit. Med. Jour.*, October 22, 1910) reports 2 cases of air embolism during labor, followed by recovery. The first was that of an apparently healthy woman, who had had one child. The second confinement was normal in the first and second stages. The patient lay on her left side in a narrow bed, with a wire mattress, which was depressed in the centre. She had a little chloroform during the later stages of delivery and was not turned upon her back until after the child had been born. When the uterus again contracted, the patient suddenly exclaimed that she was dying, became cyanosed, and had a general convulsive seizure. This passed off, and attempts were made to express the placenta, followed by uterine contraction, which caused another convulsion. The following uterine contraction produced the same result, the cyanosis became permanent, and the patient's heart greatly dilated. The placenta was removed by hand and the uterus washed out with saline solution. A pint of saline fluid was introduced into a vein in the arm, and strychnine given hypodermatically. The patient gradually improved and ultimately recovered. In the second case, the patient was a primipara and had always been delicate. Delivery was accomplished under chloroform by forceps, the perineum being somewhat torn. After the child was born the uterine contractions produced spasm, with air hunger, and frequency and irregularity of the pulse. Attempts to express the placenta caused uterine contractions and a return of the spasms. The patient's heart became markedly dilated. The placenta was removed by hand and the uterus irrigated with salt solution. No further spasmodic attacks occurred, and the patient slowly recovered.

Cesarean Section.—BOYD (*American Journal of Obstetrics*, March, 1911) reports 7 cases of Cesarean section, making his total number 27. One of these was a repeated section, the first operation having been performed about two years before the second. The uterus was found adherent to the anterior abdominal wall, and as the adhesions were not extensive the uterus was liberated. The incision was made in the median line, high up, and to the right of the old scar; convalescence proceeded smoothly, mother and child making a good recovery. Another of the operations reported was a twin pregnancy complicated by toxemia. As dietetic treatment produced no improvement the pregnancy was terminated by section. Considerable shock followed, the stomach becoming distended with gas. This was relieved by gastric lavage. Both mother and children made a good recovery. Among the total number of cases delivered were 6 of repeated Cesarean section. In one patient the operation was repeated three times; in 2 cases extensive adhesions were found, which necessitated in one case a longitudinal fundal incision, and in another a transverse fundal incision. The essentials of operation the author considers to be a careful selection of cases, a study of the fetal heart sounds before operating, and accurate closure of the uterine incision.

Perforation of the Uterus and Laceration of the Small Intestine.—WIENER (*American Journal of Obstetrics*, March, 1911) reports the

case of a multipara, who was several months pregnant, who slipped and fell in the street, striking on the buttocks. This was followed at once by abdominal pain and vaginal bleeding. The vagina was immediately packed with gauze, and the next day, as the pain and bleeding persisted, an attempt was made to empty the uterus. After the removal of a considerable mass of tissue with placental forceps, the operator observed that he had pulled a loop of intestine into the vagina. This was replaced and the uterus firmly packed. When the original packing was removed and the cervix dilated, the uterine cavity was found empty, but posteriorly on the left side close to the fundus, was a large perforation opening into the peritoneal cavity. On opening the abdomen about one quart of blood escaped. A mutilated fundus of about three months was found among the intestines. There was a ragged tear at the left cornu of the uterus, the edges of which were trimmed, and the tear closed with catgut. A loop of small intestine, 11 cm. long, was found to have been torn from its mesentery. There were two perforations into the gut. This was resected, an end-to-end anastomosis made, using a Murphy button. The abdomen was closed with a large Mikulicz drain of plain gauze in Douglas' cul-de-sac. The patient gradually recovered and left the hospital before the passage of the button. Three months after operation the patient was in good condition, and a skiagraph of the abdomen showed that the button had been passed.

Fatal Mercurial Poisoning from Bichloride Tablets used to Produce Abortion.—SCHILDECKER (*American Journal of Obstetrics*, March, 1911) reports the case of a young woman who introduced into the vagina to produce abortion six bichloride tablets, each containing 7.3 grains. This immediately produced severe and burning pain and such muscular spasm that the patient could not remove them. A physician was promptly summoned, who gave vaginal douches of warm water and morphine hypodermically. The patient speedily developed intense symptoms of mercurial poisoning, and died four days later. At autopsy an intense necrotic exfoliative enterocolitis was present, most severe in the rectum. The process was distinct as high as the duodenum. There was also necrosis of the muscular walls of the vagina and vaginal portions of the cervix. The broad ligaments, Fallopian tubes, and ovaries were necrotic, but above the internal os the lining of the uterus was normal. There was no evidence of peritonitis. Posteriorly the pelvic peritoneum was separated from the pelvic wall and distended with serum. The left kidney was cystic, containing serum, and both kidneys showed fatty degeneration. There was myocardial fatty degeneration, and apparent chematous degeneration of the liver and spleen. In a second similar case the patient was taken to the hospital and treated by continuous enteroclysis. She survived two weeks, then died in collapse. The autopsy revealed changes similar to those in the first case, with perforation in the lower third of the descending colon and general peritonitis. In a third case the patient was treated by intravaginal douches of hot water and hot milk. This patient died at the end of a week with tremors and paralysis. Autopsy showed passive hemorrhage in the peritoneal cavity and bloody serous exudate beneath the cerebral meninges.

GYNECOLOGY.

UNDER THE CHARGE OF

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A Contribution to the Treatment of Gynecological Bleeding.—HENKEL (*Münch. Med. Woch.*, 1911, lviii, 337) mentions the various local and general causes of uterine hemorrhage, but considers especially the etiology and treatment of those cases in which no pathological lesion can be demonstrated. He ascribes many cases of irregular menstruation as well as dysmenorrhœa to variations in the functional activity of the ovarian follicles. These cases may be divided into two general groups, the one exhibiting many follicles with an abnormal activity, the other an unusually small number of follicles with consequent diminution in activity. Since clinical as well as anatomical observations have shown that cyclic changes in the endometrium are dependent upon ovarian activity, it is permissible to assume that an irregularity in this activity may produce alterations in the uterine mucosa which lead to irregular bleeding. Partial resection of hyperfunctionating ovaries has in many instances, been followed by a return of the menstruation to normal and cure of dysmenorrhœa. Should the ovaries be unusually small, as detected by physical examination, he advises ovarian extract together with yohimbin and lecithin, with the idea that such treatment not only has an immediate effect in checking the bleeding, but that it also promotes further development of the ovaries. Henkel looks upon the uterus and ovaries as an integral part of the genital apparatus; removal of the one impairs the activity of the other. He therefore makes it his practice to remove both ovaries with the uterus in cases of myoma. The after-results have been no less favorable than when the ovaries were not sacrificed and the immediate postoperative results have been more satisfactory.

X-ray Treatment of Uterine Hemorrhage.—GAUSS (*Zentbl. f. Gyn.*, 1911, xxv, 394) reports the results of this form of treatment in 100 cases in the Freiburg clinic during the last two years. He discusses these cases from the standpoint of clinical effect, of duration of treatment, and of dosage. On the basis of this experience he has come to the conclusion that cases of benign uterine hemorrhage (*i. e.*, due to myomata or to metropathic conditions) which are not amenable to x-ray treatment positively do not exist, and does not hesitate to continue this form of treatment even in the presence of a secondary anemia with but 15 per cent. of hemoglobin. Of the 100 cases under consideration, 55 were definitely cured, 37 are still under treatment, all showing every prospect of reaching a definite cure, and of the others, a few stopped treatment from purely extraneous reasons, such as cost, etc.; in a few, special contraindications, such as pyelitis, insanity, were present. The cured cases fall into two classes—women

past the климаeterium, or with very large myomata; in these amenorrhea was produced; and younger women, or those with small myomata; in these a shrinkage of the tumor and a reduction but not complete cessation of menstruation was aimed at and attained. The average duration of treatment, including all interruptions, many of which were from causes in no way connected with the treatment itself, was three and one-quarter months. The dosage, reckoned on the basis of the total number of minutes that each patient was actually exposed to the rays during the entire treatment, was 234 to 307 "light minutes," according to the class of case, or, expressed in Kienbock's "X-Units," in which 10-X corresponds to an erythema-producing dose, the average of all cases was about 75-X required to produce a cure. Experience has shown that myoma cases require, other conditions being equal, a larger dosage than metropathia cases without tumor, and that cases of either class require a smaller dosage the more advanced the age of the patient, a result that was, of course, to be expected. The nearer together the sittings can be given the better seems to be the result. With the present highly developed technique very large doses can be given without bad effects, but in no case can the final result be attained in less than two months, as the injury to the ovaries produced by the x-rays does not become apparent until the first or second following menstruation.

The Appendix in Gynecology.—LEGUEU (*La Gynécologie*, 1911, xv, 145) states that he makes it a habit to remove every appendix when the abdomen has been opened, whether it appears diseased or not, provided its seeking and removal does not seriously increase the danger of the operation. He has recently examined microscopically a small series of appendices so removed in the course of gynecological operations, with the following results: Of 17 appendices removed during the course of a right-sided or double salpingectomy for salpingitis, 16 showed definite lesions, 15 of these being a peritoneal or subperitoneal inflammation, acute in character, and evidently occurring by way of the lymphatics. In some, but not all of these cases, an acute or chronic inflammation of the mucosa was also present. Of 13 appendices removed during operations for other gynecological affections (extra-uterine pregnancy, ovarian cyst, fibroids, etc.), 3 were normal; in the remaining 10 there were minor lesions without any demonstrable causal relation to the primary affection. Notwithstanding that in these cases the relation between the appendiceal lesion and the primary affection cannot be distinctly shown, as in the case of adnexal inflammations, Legueu recommends, nevertheless, that all appendices be removed in these cases as well, if merely from a prophylactic standpoint.

Compression of the Ureters in Genital Prolapse.—On the basis of two carefully studied postmortem specimens, one of partial and one of complete prolapsus uteri, HIROKAWA (*Deutsch. Zeitschr. f. Chir.*, 1911, cix, 1) has been able to show that a stagnation of the urinary flow, with dilatation of the ureters, reaching at times to the pelvis of the kidney, with the production of hydronephrosis, may occur as a result of compression of the ureters in cases of genital prolapse in woman. The point of compression is always situated in the lower

portion of the ureter, not, however, as earlier writers have assumed, merely at the point of herniation through the pelvic musculature, but also above and below this point. Inside the true pelvis compression of the ureters can be caused by pressure from the bladder, the intra-abdominal portion of which is drawn down in a more or less funnel-shaped form into the likewise funnel-shaped pelvic outlet by the cystocele below. At the hernial opening in the ring musculature of the pelvic floor the ureters are, of course, liable to compression between the uterus and the neck of the cystocele on the one hand, and the muscle on the other, while below this point they are also compressed in the chronically inflamed, inelastic tissue forming the wall of the everted vaginal tube. Another factor in causing stagnation of the flow is the sharp upward bend which the ureters have to make just before entering the bladder, owing to the fact that in cystocele cases the trigonum is as it were turned upside-down, so that the ureter can no longer enter the bladder in an axis which is more or less the direct continuation of that of the latter part of its extravescial course, as is normally the case.

Ascending Kidney Tuberculosis.—BAUEREISEN (*Zeitschr. f. Gynäkol. Urologie*, 1911, ii, 276) reports the results of some experimental studies in this subject, injecting for this purpose small doses of human tubercle bacilli into the bladders of 21 guinea-pigs. Six of these developed isolated bladder tuberculosis, demonstrated pathologically, and one animal which still survived a year after injection presented certain clinical evidence of the same condition. In 3 of the animals the infection spread to the intramural portion of the ureters. In no case did it spread higher than this and affect the upper part of the ureters or the kidneys. In 9 female animals there was no spread of the infection to the genital organs, except in one case, where the outer layers of the vaginal wall were slightly affected, whereas in practically all the male animals the genital organs showed extensive involvement. As a result of these and previous experiments, in which the bovine form of the tubercle bacillus was used, the author reaches the conclusion that infection of the bladder can occur only in the presence of a relatively large epithelial defect, but is impossible with intact epithelium. He believes, further, that with unobstructed urinary flow a tuberculous infection of the bladder cannot spread through the ureter to the kidney, although infection of the intramural portion of the ureters was found in 3 of the experimental cases, explaining this on the ground that the lymph vessels of the ureter form a closed system, the current flowing from the mucosa to the adventitia, and then through descending branches to the regional glands. The part of the bladder in connection with the ureters contains lymph vessels, however, which are in communication with those of their intramural portions, so that the tubercle bacilli are carried into the outer layer of this portion of the ureter; but a further spread must take place against the current, this being possible only when the lymph flow is interfered with in some way, as by compression of the ureter. He maintains, therefore, that catheterization of the ureters is permissible even in cases of bladder tuberculosis, if every possible care is taken to avoid injuring the epithelium, believing that even if bacilli are carried into the ureter in this way, the current of urine will easily sweep them out again.

OTOLOGY.

UNDER THE CHARGE OF

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Operative Opening of the Labyrinth.—W. WOJATSCHKEK (*Russki Wratsch*, No. 47, 1909), following an enumeration of the indications for surgical invasion of the labyrinth and a description of the operations of Bourget and Neuman, presents his own method of procedure in labyrinthotomy. The important point in the three methods of operating is the evacuation of the vestibule, which, with the ampullary extensions of the semicircular canals, presents the largest individual space in which the suppurative product of a diffuse labyrinthitis would accumulate. From the customary trepan opening into the vestibule the author chisels backward, behind the nerviduct of the facial, removing as little of the semicircular canals as possible, rather than the extensive exenteration of the canals practised by Neumann; more conservative than Neumann also in regard to the anterior portion of the labyrinth, Wojatschek saves as much of the cochlea as may be consistent with effective evacuation and drainage. In this respect Wojatschek's operation lies between those of Bourguet and Neumann. Its advantage consists in the avoidance of circumjacent injury, and its disadvantage lies in failure to open the recesses of the cochlea and semicircular canals, thus favoring the retention of septic material.

Transillumination of the Mastoid Process from the External Auditory Canal.—Since the first communication on this subject by Urbantschitsch, in 1892, methods of illumination have so changed, and that of electrical illumination especially has become so far perfected, as to add greatly to the ease with which transillumination from the body interior may be accomplished. The anatomical structure of the mastoid, as GUSTAV DITENFASS (*Archiv f. Ohrenheilkunde*, Band lxxxiii, Hef 1 and 2) demonstrated, suggests the application, to the study of its interior conditions, of those means which have already been successfully applied to other bony structures with pneumatic spaces, and the method of procedure is simple. The apparatus consists of a flexible conductor about two meters in length dividing at a sufficient distance, from one end, into two conductors, to permit of simultaneous application of the two ears of the patient. Each of those ends carries a small cylindrical electric lamp, 2 cm. long and 5 mm. in diameter, with a rounded end and constructed of the so-called cold glass, which is slow in transmitting heat and permits of long retention of the lamps in the external canals without discomfort, while, by interposition of an endoscopic rheostat, variations in the intensity of the illumination are attainable. The voltage of the lamps is from 2 to 2½, and they give a light of from 7 to 10 candle-power. With the lamps inserted in the external canals, the current should be grad-

ually increased until the maximum degree of illumination has been reached, and this may be maintained from fifteen to fifty seconds without discomfort, when the current should be gradually decreased; the simultaneous transillumination of the two mastoids giving opportunity for comparative observation. Under normal conditions, by this method of transillumination, the mastoid region exhibits a rose-colored glow outlining the mastoid process, more intense anteriorly, and gradually fading in intensity upward, downward, and backward. In the thinner and more pneumatic mastoids the illumination is more intense, while with dense bony structure, or much superincumbent fatty tissue, the coloration sinks to a dull red and the bony outline is less distinguishable. The portion of the mastoid process comprising pneumatic cells transmits the light from the external canals most perfectly, sclerotic or eburnized bone much less, while pus, granulation tissue, and cholesteatomatous masses are comparatively obstructive and their presence is indicated by the shadows in the illuminated field. The clinical value of this method of simultaneous transillumination of both mastoids consists in the opportunity it affords for comparison where the disease is unilateral, and as a control examination for the determination of the location of light obstructive elements in the mastoid contents, simple hyperemia of the bone being evidenced by a diffuse diminution of the transillumination.

Investigations Concerning Disturbances of Hearing in the Artillery Service.—As the result of his observations, JAEHNE (*Zeitschrift f. Ohrenheilkunde*, lxii, 111) arrives at the conclusion that members of the foot artillery, of several years' service, are the subjects of a permanent impairment of hearing, as the result of the effect of exposure to loud noise upon the auditory nerve in its terminal distributions. Pathologically, the disturbance is to be regarded as a degenerative neuritis, the clinical symptoms, in the majority of cases, being an impairment of hearing for tones in the fourth and fifth ledger octaves, either with or without diminution of the upper tone limit. The medium for transmission of the injurious sound waves was mainly the craniotympanal rather than the aërial, except in instances in which the soldier stood near the muzzle of the gun in firing, and the author advises protection by interposition of acoustically opaque bodies, as well as the customary stopping of the external canals. Passow, in his treatise upon injuries of the ear, quotes Mueller, who examined 51 artillerymen both before and after artillery practice with heavy guns, and found that in 40 cases the duration of hearing for the tuning fork was perceptibly shorter immediately after the gun practice than before. Marked shortening of the duration of hearing by bone conduction, without corresponding impairment of aërial hearing, is also observable in paralytics, alcoholics, and epileptics, as well as in cases of dural adhesions. A similar decrease is observable in cases of hysterical deafness and in persons of advanced years. In labyrinth injury, where the hearing is noticeably impaired for sounds aërially conveyed, the higher tones are usually heard less, proportionately, than tones of low pitch, and in some cases this difference is striking; even where the impairment of the general hearing is slight the loss of hearing for the higher tones is pronounced, as has been determined by

Bezold in his tests of sharpshooters and hunters, by means of Galton whistles, the left ear being more commonly affected because of its greater exposure to concussion in the use of fire arms. A corresponding decrease in the hearing of high tones has also been observed by Buerchner, in locomotive engineers and firemen, by Habermann, in boilermakers and machinists, and by Gradenigo, in stonemasons and millers. If the upper tone limit (normal, 45,000 v. s.) is lowered, or the duration of hearing for high tones materially decreased, it may be assumed that the hearing for the remaining tones in the scale of audition is not absolutely normal; the larger the participation of the perceptive portion of the labyrinth in an injury, the more the auditory nerve is restricted in its function, the greater will be the limitation of the auditory field; while, in the majority of cases of labyrinth concussion, it is the basis of the cochlea that is injured, it does not follow that remaining portions of the cochlea are similarly implicated, and, if limited portions, or even single fibers, of the auditory nerve remain uninjured, there will be the tone islands and tone spaces described by Bezold; Baginsky, by experiments on dogs, has established the fact, confirmatory of the Helmholtz theory, that after destruction of the base of the cochlea the animals responded only to tones of low pitch, and after destruction of the upper portion of the cochlea, only to tones of high pitch.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Pellagra and its Relation to Maize.—RAUBITSCHKE (*Berliner klin. Wochenschr.*, June, 1910, xxiii, No. 26) seems to have been the first to take up in an experimental way the question as to the effects of exposure to sunlight upon maize-fed animals in association with the question of a possible relation to the etiology of pellagra. Raubitschek furnishes in a recent paper (*Centralbl. f. Bakt.*, 1 Abt., Orig., Band lvii, Heft 3) more detailed experiments which throw important light upon this subject. He notes the immense amount of literature which has accumulated on the etiology of pellagra and condemns severely the very questionable kind of work which has been done in this field. He also comments upon the scanty results of pathologico-anatomical work upon this disease and that modern microbiological, especially serological technique has not to any extent been used in clearing up its etiology. The theories of the etiology of pellagra are considered in three groups—the bacterial, the toxic, and the auto-toxic, none of which in its present state can be considered satisfactory. Lavinder points out that Raubitschek fails to take note of the more

recent views of a protozoal origin of pellagra. The warning is probably made that if the real cause of pellagra is unknown we must not insist too closely upon bringing the disease into strict causal relation with the use of maize as a food and that if any real progress is to be made the above theories must be tested in a satisfactory experimental way especially upon pellagrins before they can be accepted as of real importance. Raubitschek found it possible to study only briefly the numerous microorganisms which have been isolated from both good and spoiled corn of various workers and presented as the cause of pellagra. Since raw corn is not directly consumed, he deemed the bacteriological investigation of prepared (cooked) food worthy of more consideration than the raw material. He prepared polenta and cakes from both good and bad corn and in a few cases recovered some species of *penicillium* and *aspergillus*, but chiefly the *bacterium maidis*. Usually his cultures were sterile. Blood cultures from the arm vein from pellagrins in all stages of the malady proved constantly and invariably negative. He occasionally found the *bacterium maidis* in pellagra stools. He obtained negative results from the organs a few hours after death. He concluded, therefore, that there exists no basis for a parasitic etiology of the pellagra. Along serological biological lines, Raubitschek looked for a precipitin reaction in the blood serum of pellagrins in all stages of the disease with extracts of maize. The results were always positive. He obtained, however, the same precipitation with both healthy persons and animals. He obtained nothing characteristic with the complement-fixation reaction and negative results in experiments for hypersusceptibility in pellagrins and in healthy persons by means of the ophthalmo- and cutaneo-reactions with various maize extracts. Numerous other experiments upon the phenomena of anaphylaxis in relation to maize antibodies were attempted. He concludes from the work of this section that antibodies specific for maize albumins (both good and bad maize) do not occur in the serum of pellagrins. Raubitschek obtained various extracts from both naturally or artificially spoiled maize which he injected into rabbits, mice, and guinea-pigs in various amounts. These experiments were negative, as were also feeding experiments with these substances. The author then points out that the pellagrous erythema is usually confined to an exposed surface of the body, and thinks that from this it may be inferred either that there is a reduced resistance of the entire body surface and hence exposed parts are unduly sensitive to slight noxious influences as sunlight, or that the influences of a maize diet, in the body surface exposed to sunlight there is developed a noxious substance (Noxe) which produces not only local morbid changes, but also affects the entire organism. It is possible that there may be some relation between a maize diet, sunlight, and pellagra, and reference is made to the work of Asehoff and to the fact that the usual occurrence of pellagra skin changes occur that season when the field laborer is most exposed to the sun. He shows that in buckwheat poisoning (fagopyrismus) in white or spotted animals exposed to light suffer while dark animals or white animals kept in the dark escape. The active photodynamic substance of buckwheat is soluble in organic solvents and seems to be a fat or lipid. Numerous experiments are shown demonstrating and corroborating these facts. Raubitschek con-

cludes that he has demonstrated the presence of a photodynamic substance in maize and that this material is soluble in alcohol. He does not attempt to bring his experimental results into a strict relation with the etiology of pellagra or to assume for this disease a photodynamic basis, or even to conclude that pellagra is produced by an almost exclusive diet of maize (good or bad). This inference, however, is suggested. Attention is drawn to the effect of a rice diet in animals and the fact that this cereal is also rich in fat and by many is held accountable for a somewhat analogous disease to pellagra, viz., beriberi. Raubitschek finally calls attention to the fact that the possibility should be borne in mind that pellagra and pellagroid affections may be due not only to the use of maize as a food but also to the use of other grains and other plant stuffs which are eaten in various localities. LAVINDER (*Public Health Reports*, May 5, 1911) has recently repeated these experiments upon rabbits, guinea-pigs, mice, and rats, with negative results.

The Subsequent Health of Children who Drank Milk Containing Tubercle Bacilli.—HESS (*Jour. Amer. Med. Assoc.*, 1911, li, 1322 to 1324) has continued his studies upon tubercle bacilli in milk. He has made a systematic examination of 18 children covering a period of three years. These children, three years ago, drank milk which was shown to have contained virulent tubercle bacilli. Of the 18 children who drank this milk in which tubercle bacilli were demonstrated, all but one remained free from active tuberculosis during the period of supervision, viz., three years. The one case developing tuberculosis showed tuberculous lesions of the cervical glands in which a bacillus of the bovine type was cultivated. He concludes that tubercle bacilli in milk are a menace to the health of young children. Tubercle bacilli in butter are likewise a menace, therefore safe butter, whether pasteurized or certified, should be provided for their use.

CORRIGENDA

Page 697, read paragraph 3 following Table V

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